ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE ENGINEERING AND TECHNOLOGY

MAIN CHAIN POST-FUNCTIONALIZATION OF SYNTHETIC POLYESTERS THROUGH DIELS-ALDER CYCLOADDITION REACTIONS

M.Sc. THESIS

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Department of Chemistry

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İSTANBUL TEKNİK ÜNİVERSİTESİ ★ FEN BİLİMLERİ ENSTİTÜSÜ

DIELS-ALDER SİKLO KATILMA REAKSİYONLARI İLE SENTETİK POLİESTERLERİN ANA ZİNCİRİNİN FONKSİYONLANDIRILMASI

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To my beloved family,

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ABBREVIATIONS

°C	**:** Celsius
^{1}H NMR	: Hydrogen Nuclear Magnetic Resonance Spectroscopy
^{13}C NMR	: Carbon Nuclear Magnetic Resonance Spectroscopy
DA	: Diels-Alder
FPT	: Freeze-Pump-Thaw
GPC	: Gel Permeation Chromatography
p-TSA	: *p*-Toluenesulfonic acid
THF	: Tetrahydrofuran

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MAIN CHAIN POST-FUNCTIONALIZATION OF SYNTHETIC POLYESTERS THROUGH DIELS-ALDER CYCLOADDITION REACTIONS

SUMMARY

Polymer chemistry generally requires high-yield and highly specific chemical reactions [1]. In that context, it comes as no surprise that modular reactions of the "click"-type [2] have recently been gaining popularity in polymer science. In 2001, Sharpless and coworkers introduced "click" chemistry, a new approach in organic synthesis that involves a collection of almost perfect chemical reactions. Nowadays there are several processes have been identified under this term in order to meet Sharpless's criteria. Among those selected reactions, copper(I)-catalyzed azidealkyne (CuAAC), active ester substitution reactions and Diels-Alder (DA) cycloaddition reactions are also described in many published articles.

Diels-Alder (DA) reaction is one of the most common reactions used in organic chemistry, and invented by Otto Diels and Kurt Alder who received the Nobel Prize in 1950 for their discovery. The Diels-Alder reaction is a concerted [4π+2π] cycloaddition reaction of a conjugated diene and a dienophile to yield a 6-membered ring. This reaction is one of the most powerful tools used in the synthesis of important organic molecules in high yields.

The Retro-Diels–Alder reaction (rDA) is the microscopic reverse of the Diels–Alder reaction the formation of a diene and dienophile from a cyclohexene. It can be accomplished spontaneously with heat, or with acid or base mediation [3]. If a Diels-Alder adduct is heated at a much higher temperature than the temperature at which it forms in a Diels-Alder reaction, it breaks down to give the diene and the dienophile. Retro Diels-Alder reaction is a pericyclic reaction.

Before the development of click chemistry, the first triazole synthesis, from diethyl acetylenedicarboxylate and phenyl azide, was reported by Arthur Michael in 1893. Later, 1,3-Dipolar cycloaddition reaction mechanism and synthetic application were established by Rolf Huisgen in 1960. A disadvantage of this reaction is that it is relatively slow and requires high temperatures to give acceptable yields. However, in the presence of catalytic amounts of Cu(I), the reaction is highly efficient and regioselective and proceeds under mild conditions. In 2002, the copper-catalyzed azide-alkyne cycloaddition (CuAAC) was independently developed by Sharpless and coworkers [4]. This version gives only the 1,4-isomer, whereas Huisgen's non-catalyzed 1,3-dipolar cycloaddition gives both the 1,4- and 1,5-isomers, is slow, and requires a high temperature as mentioned [5].

Afterwards, Bio-orthogonal reaction was developed by Carolyn R. Bertozzi in 2003. This reaction can be describe as activated varient of Huisgen type of reaction and based on the work by Sharpless and coworkers. Cu-free click chemistry has been modified to be bio-orthogonal by eliminating a cytotoxic copper catalyst, allowing reaction to proceed quickly and without live cell toxicity [6]. Instead of copper, the

reaction is a strain-promoted alkyne-azide cycloaddition (SPAAC). This reaction uses the release of ring strain energy of a cyclooctyne group as a consequence of the geometrical deformation of the triple bond, to enable the 1,3-dipolar cycloaddition to proceed rapidly without the need of a metal catalyst [7]. This reaction has enabled the study of biomolecules such as gylcans, proteins[8] and lipids[9] in real time in living systems.

Polyester is a type of polymers which is including the ester functional group in their main chain. Polyethylene terephthalate (PET) is the well-known name for the industry. Depending on a chemical structure, polyester can be a thermoplastic or thermoset. Polyester production is very important because it can be used of the wide range of the area from clothing to cover,to plastic and bio-degredable materials. It can be sytnthesis by condensation polymerization or ring opening polymerization.

In this study we prepared a series of polyesters containing electron deficient internal alkyne units derived from acetylene dicarboxylic acid in the main backbone. This Next, one of polyesters was employed as a polymeric platform in copper free cycloaddition reactions like Diels-Alder cycloaddition reactions in the presence of various dienes, respectively. The Diels-Alder cycloaddition reactions were carried out at higher temperatures (60 to120 ^{o}C) in 1,4-dioxane for 16 h with reasonable efficiencies (45-97%). Moreover, the furan-adduct polyester was successfully used in 1,3-dipolar cycloaddition/retro-Diels-Alder reactions in the presence of dipolar. All characterization processes are made by using GPC, ^{1}H NMR, ^{13}C NMR.

DIELS-ALDER SİKLO KATILMA REAKSİYONLARI İLE SENTETİK POLİESTERLERİN ANA ZİNCİRİNİN FONKSİYONLANDIRILMASI

ÖZET

Polimer kimyası genellikle yüksek verim ve yüksek oranda spesifik kimyasal reaksiyonlar gerektirir [1]. Bu bağlamda, "click" tipindeki [2] modüler reaksiyonların polimer biliminde son zamanlarda popülerlik kazanması sürpriz olmadı. 2001 yılında Sharpless ve çalışma arkadaşları "click" kimyası başlığı altında organik sentezler için neredeyse mükemmel kimyasal reaksiyonlar derlemesi içeren yayınlarını yayınlamışlardır. Sharpless, farklı reaksiyonların "click" reaksiyonları olarak tanımlanabilmesi için bu reaksiyonların yerine getirmesi gereken bir takım kriterler de sıralamıştır. Bu reaksiyonların arasında Cu (I) katalizörlüğünde azid-alkin siklokatılma reaksiyonu (CuAAC), Diels-Alder (DA) reaksiyonu bulunmaktadır ve bir çok makalede de bahsedilmişlerdir.

Diels-Alder (DA) reaksiyonu organik bileşiklerde en yaygın reaksiyonlardan biridir. 1950' de Otto Diels ve Kurt Alder bu keşifleri sayesinde Nobel Ödülü kazanmışlardır. Diels-Alder reaksiyonu, 6 üyeli bir halka oluşturmak üzere bir konjüge dien ve bir dienofilin uyumu sonucu gerçekleşen [4π + 2π] sikloadisyon reaksiyonudur. Bu reaksiyon, önemli organik moleküllerin yüksek verimde sentezinde kullanılan en güçlü araçlardan biridir.

Retro-Diels-Alder reaksiyonu (rDA) Diels-Alder reaksiyonunun mikroskobik olarak tersidir ve bir sikloheksenden bir dien ve dienofil oluşturur. Isıl, asit veya baz arabuluculuğu ile spontan olarak gerçekleştirilebilir [3]. Bir Diels-Alder ürünü, bir Diels-Alder reaksiyonunda oluştuğu sıcaklıktan daha yüksek bir sıcaklıkta ısıtılırsa, dien ve dienofili vermek üzere parçalanır. Retro Diels-Alder reaksiyonu perisiklik bir reaksiyondur.

Geçen yüzyılın ortaları, fiziksel organik kimya için altın çağıydı.Yapının ve reaktivitenin temel ilişkisini anlamanın amacı, başka hiçbir algılanan faydası olmayan bileşiklerin geniş bir yelpazesini sentezlemek için yeterli gerekçeydi. Kimyadaki eğilimler değiştikçe, uygulama temelli hedeflere odaklanıldığından, Huisgen ve Krebs gibi kimyagerlerin bulgularının çoğunun, çoğunlukla bakır katalizli azid-alkin siklo eklenmesi biçiminde bir rönesans yaşayana kadar, çoğunlukla akademik öğretme araçları oldukları söyleniyordu. Bu, malzeme bilimlerinden biyokimyaya, daha eski literatüre dağılmış reaksiyonların hazine sandığına uzanan araştırmacılar ile kimyasal topluma enerji sağlamıştır.

'Click' kimyası tanıtılmadan önce, dietil asetilenkarboksilat ve fenil azid ile gerçekleştirilen ilk triazol sentezi, Arthur Michael tarafından 1893'te geliştirildi. Daha sonra, 1,3-Dipolar sikloadilasyon reaksiyon mekanizması ve sentetik uygulama, Rolf Huisgen tarafından 1960 yılında ortaya çıktı. Bu reaksiyonun bir dezavantajı, nispeten yavaş olması ve kabul edilebilir verim vermesi için yüksek sıcaklıklara ihtiyaç duymasıdır. Bununla birlikte, katalitik miktarda Cu (I) varlığında, reaksiyon oldukça verimli, regioselective ve yumuşak koşullar altında ilerlemektedir.

2002'de, bakır katalizli azid-alkin sikloadksiyonu (CuAAC), Sharpless ve iş arkadaşları tarafından bağımsız olarak geliştirildi [4]. Bu versiyon sadece 1,4-izomer verirken, Huisgen'in katalize edilmemiş 1,3-dipolar sikloadizasyonu hem 1,4 hem de 1,5 izomerleri verir, yavaştır ve bahsedilen yüksek sıcaklık gerektirir [5].

'Click'reaksiyonları, seçici olma, yüksek verime sahip olma ve iyi reaksiyon kinetiğine sahip olmak gibi avantajlara sahiptir. Bileşenleri çevreleyen biyolojik ortama inert olan 'Click' reaksiyonlarının bir alt sınıfı, biyo-ortogol'dir. Bu reaksiyon biyolojik uyumluluğun eklenen komplikasyonları nedeniyle 'Click' reaksiyonunun tipik tanımının ötesinde onu bir adım daha ilerletmiştir.

Son yıllarda, Sharpless ve arkadaşları azidler ve alkin ya da nitriller arasındaki Huisgen 1,3-dipolar siklokatılmalarda ([3 + 2] sistemi) Cu(I)'i baz ile birleştirip kataliz olarak kullandılar ve bu reaksiyonu click reaksiyonu olarak adlandırdılar. Siklo katılma reaksiyonları, çevrimsel yükler, ayarlanabilir elektronik ve özünde seçicilikleri nedeniyle ideal reaksiyonlar olarak görülüyordu. Huisgen, azid ve asiklik bir alkin arasında [3 + 2] sikloadizasyonu geliştirdi ancak bu reaksiyon, Triazolü oluşturmak için alkin bağ açısı deformasyonun aktivasyon bariyerini aşmak için ısıya ihtiyaç duydu. Sharpless ve iş arkadaşları, bu reaksiyonun substrat olarak terminal alkinler kullanılarak Cu ile katalize edilmiş halini geliştirdiler ancak metalin sitotoksisitesi, canlı sistemlerdeki kullanımını sınırladığı için canlı sistem üzerinde kullanımı ve sürekliliği açısından tam olarak yeterli olmamıştı.

Click kimyası blok kopolimerlerden karmaşık makromoleküler yapılara kadar değişen birçok polimerik malzemenin yapılmasına kadar makromolekül kimyasında başarılı bir şekilde uygulandı. Click reaksiyonları, yan reaksiyonlara sebebiyet vermeyecek ve ilave saflaştırma işlemlerine gereksinim duyulmayacak bir şekilde kantitatif verimle C–C (veya C–N) bağ oluşumuna izin vermektedir.

Bu gelişmelerin ardından, Biyo-ortogonal reaksiyon Carolyn R. Bertozzi tarafından 2003 yılında geliştirildi. Bu reaksiyon, Huisgen reaksiyon türünün aktive edilmiş varyantı olarak tanımlanakla birlikte Sharpless ve iş arkadaşlarının eserine dayalıdır. Bakır içermeyen 'click' kimyası, sitotoksik bakır katalizörünü ortadan kaldırarak biyo-ortogonal olacak şekilde modifiye edilmiş ve reaksiyonun hızlı bir şekilde canlı hücre toksisitesi olmadan gerçekleştirilmesine izin verilmiştir [6]. Bakırın yerine reaksiyon, halka gerilmesine dayanan azid-alkin siklo katılma reaksiyonudur (SPAAC). Bu reaksiyon, bir metal katalizöre ihtiyaç duymadan 1,3-dipolar sikloadizasyonun hızlı bir şekilde ilerlemesini sağlamak için üçlü bağın geometrik deformasyonunun bir sonucu olarak bir siklooksit grubunun halka gerilme enerjisinin serbest bırakılmasını kullanır [5]. Bu reaksiyon, canlı sistemlerdeki glikanlar, proteinler [8] ve lipidler [9] gibi biyomoleküllerin gerçek zamanlı olarak incelenmesini sağlamıştır.

Azid, en yaygın Biyo-ortogonal fonksiyon gruplarından biridir. Küçük yapısı ve endojenik özelliğine ek olarak fosfinler ve alkinler ile çok rahat bir şekilde biyo-ortogonal olarak uyum sağlaması sebebiyle önem kazanmıştır.

Poliesterler, özellikle de alifatik poliesterler, çıkış bileşiklerinin zenginliği, sentetik anlamda daha kolay ve daha fazla alternatifi olmasından dolayı daha düşük maliyetli, ayrıca sahip oldukları ester yapısından dolayı (biyo)bozunurluluk ve biyouyumluluk özellikleri gösterdiği için de son derece çevre dostu yapılardır. Bu üstün özellikleri poliesterleri, kontrollü ilaç salınımı ve gen mühendisliği gibi birçok biyomedikal uygulamadan, yeni nesil çevre dostu tekstil ve ev araç-gereçlerine kadar geniş bir yelpazede vazgeçilmez hale getirmiştir. Diğer yandan, bu önemli özelliklerine rağmen poliesterlerden, daha da üstün özelliklere sahip yeni malzemeler elde edilmesi noktasında fonksiyonlandırılabilmesi her zaman arzu edilmektedir. Literatürde bu amaçla: i) fonksiyonel grup içeren halkalı esterlerin (lakton, laktid, glikolid vb.) halka açılma polimerleşmesi (ROP) ile polimerizasyonu ile yan zincirinde fonksiyonel gruba sahip poliester sentezi, ii) fonksiyonel gruba sahip bir diol ve/veya diasitin yüksek sıcaklıkta ortamdan su uzaklaştırılması olarak bilinen klasik poliesterleşme yöntemleri ilk akla gelenlerdir. Bunun yanında, bahsedilen bu yöntemler fonksiyonel grubun bir amaca dönük olarak önceden monomer üzerinde hazırlanması veya monomer seçiminin hangi amaç hedeflenmişse ona göre belirlenmesi gibi zorunlulukları da içerisinde barındırmaktadır.

Polyester, ana zincirinde ester grubu içeren bir polimer türüdür. Polietilen tereftalat (PET), endüstrideki yaygın adıdır. Azidlerin, bir ester ile donatılmış triarilfosfinler ile reaksiyonu - Staudinger bağlanması olarak adlandırılan bir işlem - canlı sistemlerde şimdiye kadar yapılmış ilk biyo-algılama reaksiyonudur.

Kimyasal yapısına bağlı olarak, polyester termoplastik veya termoset olabilir. Polyester üretimi çok önemlidir; çünkü giyimden kaplamaya, plastikten biyo-degredilebilir malzemelere kadar geniş bir yelpazede kullanılabilirler. Kondenzasyon polimerizasyonu ya da halka açılma polimerizasyonu ile sentezlenebilirler.

Biyouyumlu, biyodegrede olabilen ve çözünebilen polimerler, biyomedikal ve çevre bilimi alanlarındaki yüksek uygulanabilirlikleri ve kullanılabilirlikleri sayesinde medikal implantlarda ve ilaç kimyasında vücuda taşıyı vektörler olarak kullanılması hususunda önemli yer almaktadırlar.

Çevreye uyumlu ve zarar vermeyen yeni teknolojilerin keşfedilebilmesi için polimerlerin bir kolu olan poliesterlerin fonksiyonlarının geliştirilmesi çok önemlidir. Poliesterler akademi ve sanayi tarafından çalışılan ve önem arzeden polimerler olduğundan ötürü, bu gelişim, teknolojinin farklı farklı alanlarında (tekstil, otomotiv, medikal, kaplamalar, vb.) kullanılan poliesterlerin insanlığa daha iyi hizmet etmesinde rol oynayacaktır.

Bu çalışmada ana zincirde asetilen dikarboksilik asitten türetilen elektronca fakir iç alkin birimleri içeren bir dizi polyester hazırlandı. Dört farklı diol kullanılarak dört farklı poliester elde edildi. Aralarından Butanediol ile elde edilen polyester model polyester olarak seçildi. Ardından, model polyester sırasıyla çeşitli dienlerin varlığında bakır katalizörsüz Diels-Alder siklo katılma reaksiyonları için platform olarak kullanıldı. Diels-Alder siklo katkılama reaksiyonları 1,4-dioksan içinde 16 saat makul verimlilikle (% 45-97) ve yüksek sıcaklıklarda (60 ila 120 ^{o}C) gerçekleştirildi. Daha sonra furan-fonksiyonlu poliester, dipolar ile muamele edilerek 1,3-Dipolar Siklo Katılma/Retro-Diels-Alder reaksiyonunu başarıyla gerçekleştirdi. Bu reaksiyon sırasında herhangi bir katalizör kullanılmamış olup oda sıcaklığında gerçekleştirilmişir. Model poliester üzerine Benzil azid eklenerek triazol halkası oluşumu gerçekleşirken furan halkasının yapıdan ayrılarak benzil azid fonksiyonlu poliester zinciri elde edilmiştir. Tüm karakterizasyon işlemleri GPC, ^{1}H NMR, ^{13}C NMR kullanılarak gerçekleştirildi.

1. INTRODUCTION

The term of 'Polyester' is a category of polymers that contain the ester functional group in their main chain. In 1926, W.H. Carothers discovered that alcohols and carboxyl acids could be successfully mixed to create fibers. In the years 1939-41, John Rex Whinfield and James Tennant Dickson investigated polyesters and in 1941 produced and patented the first polyester fibre which they named Terylene, also known as Dacron, equal to or surpassing nylon in toughness and resilience [10]. Three reactions are generally used for the sythesis of polyesters. First is the polyesterification of dicarboxylic acids with diols or their functional derivatives; Second is self-polyesterification reaction of hydrocarboxylic acids and their derivatives; Third is ring opening polymerization reactions of lactones and cyclic esters [11]. Polyesters involve naturally occurring chemicals, as well as synthetics through step-growth polymerization. This material is used very widely in textile, plastic, film and resin industries [11]. Natural polyesters and a few synthetic ones are biodegradable, but most synthetic polyesters are not [11].

The click reactions are defined to have high yields, simple purification methods, stereo-/regioselectivity and display tolerance to various functional groups under mild reaction conditions in a wide range of solvents [12,13]. The emergence of click reactions created a new paradigm covering the orthogonal combination and functionalization of reactive polymer precursors in synthetic polymer chemistry [14-24]. The Cu(I) catalyzed azide-alkyne cycloaddition (CuAAC) fulfilling these requirements is by far the most utilized click reaction in the field of polymer chemistry [14,15,17-24]. As the CuAAC holds several advantages based on efficient polymer-polymer conjugation and easily attainable functional end-groups using a variety of controlled radical polymerizations, in addition to other advantages of click reactions.

Despite its unique features, the CuAAC has a drawback regarding the removal of copper catalyst. Furthermore, in some crucial experiments related to the biological media, the CuAAC is not a suitable reaction owing to its toxicity. Therefore, chemists have searched for alternative metal free reactions and gained them to the literature [18-

36]. Indeed, those alternatives have made an important contribution mainly to the postfunctionalization of polymer backbone [25-27]. However, most of these reactions have failed at the efficient combination of individual polymer blocks leading to complex macromolecular structures. In this regard, metal free cycloaddition reactions have been proven to be the best alternative to replace the CuAAC by several studies like Diels-Alder [16,28-31], triazolinedione (TAD) [32,33], tetrazine-norbornene [34], and strain promoted azide alkyne cycloaddition (SPAAC) reactions [35,36].

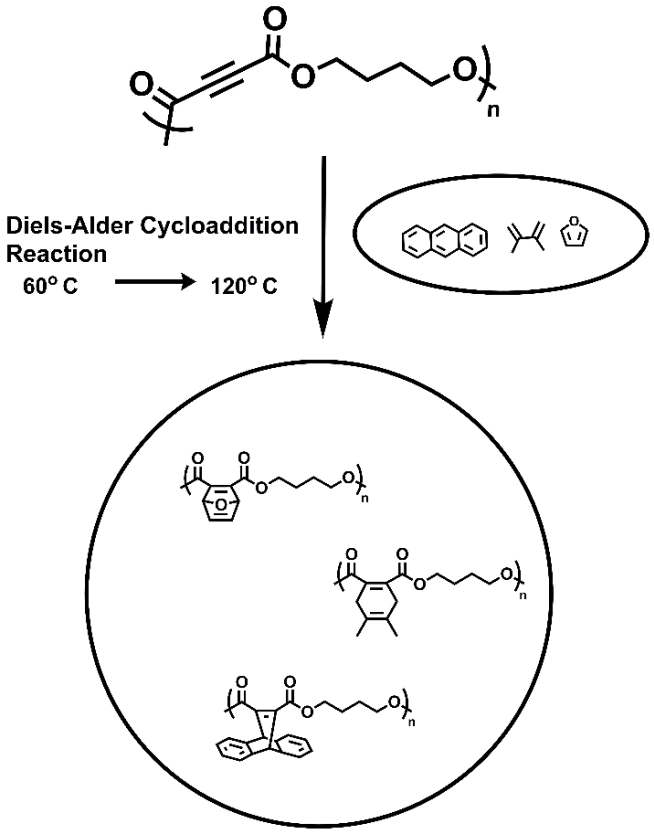


Figure 1.1: Diels-Alder cycloaddition reactions of electron deficient alkyne containing polyester **P1**.

More recently, we have focused on the structure of dialkyl acetylenedicarboxylate which has a unique feature; reactive triple bond possessing the capability of undergoing a variety of organic reactions such as nucleophilic and radicalic additions as well as multicomponent reaction (MCR) [37,38]. Besides, two carbonyl units in the structure makes the triple bond very electron deficient and suitable for cycloaddition reactions. While the triple bond act as a dienophile for Diels-Alder cycloaddition

reactions (Figure 1.1) 1, furan-functionalized polymer act as a dipolarophile for Retro-Diels-Alder reaction with addition of azide-functionalized dipolar, respectively (Figure1.2)[39].

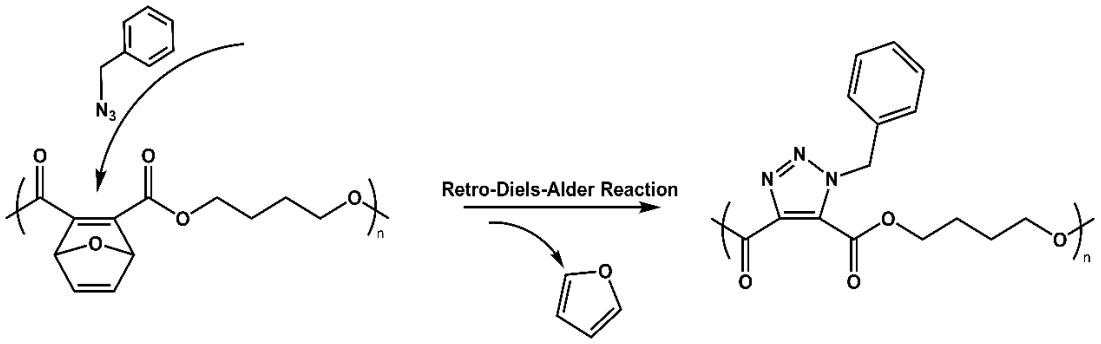


Figure 1.2: Retro-Diels-Alder reactions of furan adduct **P8**.

2. THEORETICAL PART

2.1 Condensation Polymerization

A large number of important and useful polymeric materials are not formed by chain-growth processes involving reactive species such as radicals, but they proceed instead by conventional functional group transformations of polyfunctional reactants. These polymerizations often occur with the loss of a small byproduct (which even no loss of any byproduct in this thesis' synthesis of polyurethane), such as water, and generally combine two different components in an alternating structure. The polyester Dacron and the polyamide Nylon 66, shown below (figure 2.1), are two examples of synthetic condensation polymers, also known as step-growth polymers. In contrast to chain-growth polymers, most of which grow by carbon-carbon bond formation, step-growth polymers generally grow by carbon-heteroatom bond formation (C-O & C-N in Dacron & Nylon, respectively). Although polymers of this kind might be considered to be alternating copolymers, the repeating monomeric unit is usually defined as a combined moiety [40].

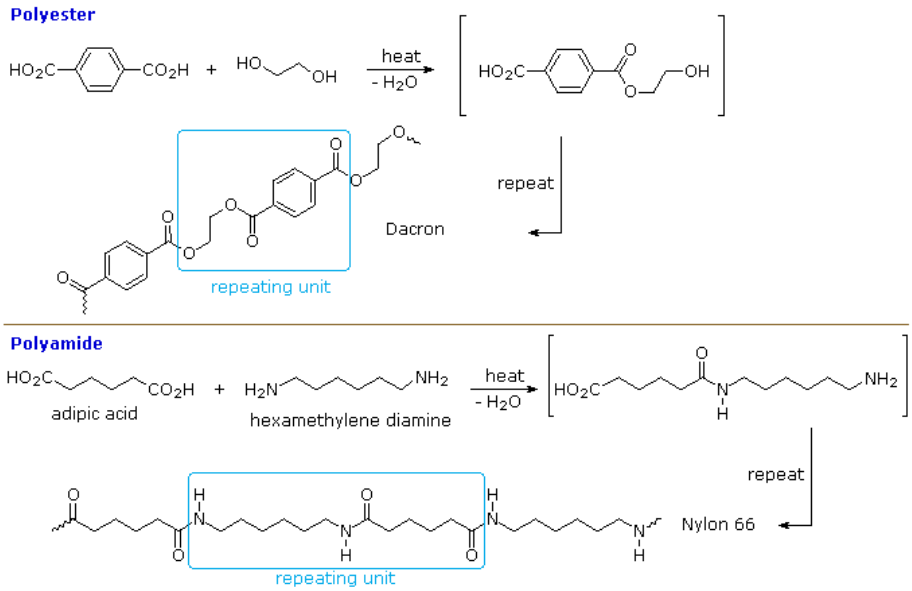


Figure 2.1: Two examples of synthetic condensation polymers.

Examples of naturally occurring condensation polymers are cellulose, a polypeptide chain of proteins, and poly(β-hydroxybutyric acid), a polyester synthesized in large quantity by certain soil and water bacteria. Formulas for these are provided below.

Condensation polymers form more slowly than addition polymers, often requiring heat, and they are generally lower in molecular weight. The terminal functional groups on a chain remain active, so that groups of shorter chains combine into longer chains in the late stages of polymerization. The presence of polar functional groups on the chains often enhances chain-chain attractions, particularly if these involve hydrogen bonding, and thereby, crystallinity and tensile strength. The following examples of condensation polymers are illustrative.

Note that for commercial synthesis the carboxylic acid components may actually be employed in the form of derivatives such as simple esters. Also, the polymerization reactions for Nylon 6 and Spandex do not proceed by elimination of water or other small molecules. Nevertheless, the polymer clearly forms by a step-growth process.

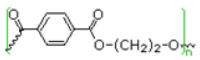
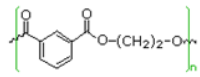
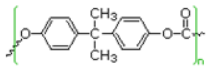
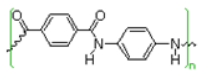
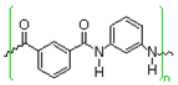
Formula	Type	Components	T_g ºC	T_m ºC
~[CO(CH$_2$)$_4$CO-OCH$_2$CH$_2$O]$_n$~	**polyester**	HO$_2$C-(CH$_2$)$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	< 0	50
	**polyester** Dacron, Mylar	para HO$_2$C-C$_6$H$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	70	265
	**polyester**	meta HO$_2$C-C$_6$H$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	50	240
	**polycarbonate** Lexan	(HO-C$_6$H$_4$-)$_2$C(CH$_3$)$_2$ (Bisphenol A) X$_2$C=O (X = OCH$_3$ or Cl)	150	267
~[CO(CH$_2$)$_4$CO-NH(CH$_2$)$_6$NH]$_n$~	**polyamide** Nylon 66	HO$_2$C-(CH$_2$)$_4$-CO$_2$H H$_2$N-(CH$_2$)$_6$-NH$_2$	45	265
~[CO(CH$_2$)$_5$NH]$_n$~	**polyamide** Nylon 6 Perlon		53	223
	**polyamide** Kevlar	para HO$_2$C-C$_6$H$_4$-CO$_2$H para H$_2$N-C$_6$H$_4$-NH$_2$	---	500
	**polyamide** Nomex	meta HO$_2$C-C$_6$H$_4$-CO$_2$H meta H$_2$N-C$_6$H$_4$-NH$_2$	273	390

Figure 2.2: Some Condensation Polymers.

The difference in Tg and Tm between the first polyester (completely aliphatic) and the two nylon polyamides (5th & 6th entries) shows the effect of intra-chain hydrogen bonding on crystallinity in Figure 2.2 and Figure 2.3. The replacement of flexible alkylidene links with rigid benzene rings also stiffens the polymer chain, leading to increased crystalline character, as demonstrated for polyesters (entries 1, 2 &3) and polyamides (entries 5, 6, 7 & 8). The high T_g and T_m values for the amorphous polymer Lexan are consistent with its brilliant transparency and glass-like rigidity. Kevlar and Nomex are extremely tough and resistant materials, which find use in bullet-proof vests and fire resistant clothing [40].

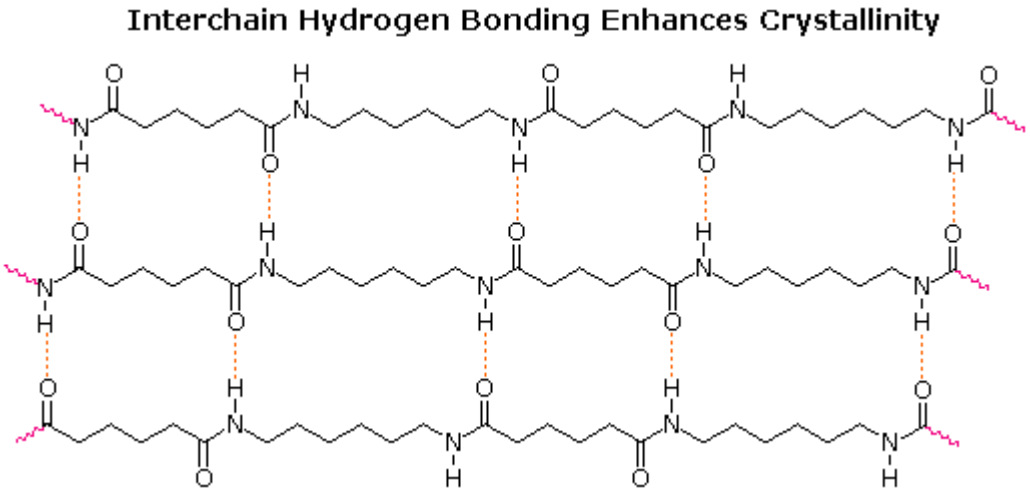


Figure 2.3: Enhancement of crystallinity by hydrogen bonding.

Many polymers, both addition and condensation, are used as fibers. The chief methods of spinning synthetic polymers into fibers are from melts or viscous solutions. Polyesters, polyamides, and polyolefins are usually spun from melts, provided the Tm is not too high. Polyacrylates suffer thermal degradation and are therefore spun from solution in a volatile solvent. Cold-drawing is an important physical treatment that improves the strength and appearance of these polymer fibers. At temperatures above T_g, a thicker than desired fiber can be forcibly stretched to many times its length; and in so doing the polymer chains become untangled, and tend to align in a parallel fashion. This cold-drawing procedure organizes randomly oriented crystalline domains shown in Figure 2.4, and also aligns amorphous domains so they become more crystalline. In these cases, the physically oriented morphology is stabilized and retained in the final product. This contrasts with elastomeric polymers, for which the stretched or aligned morphology is unstable relative to the amorphous random coil

morphology. This cold-drawing treatment may also be used to treat polymer films (*e.g.* Mylar & Saran) as well as fibers.

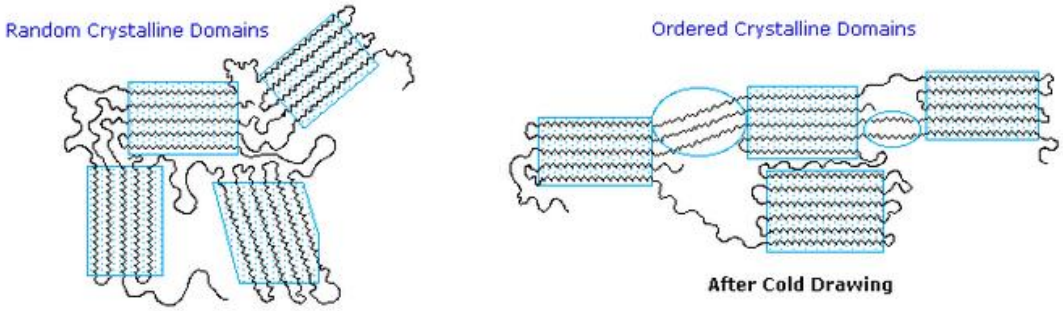


Figure 2.4: Types of crystalline domains.

Step-growth polymerization is also used for preparing a class of adhesives and amorphous solids called epoxy resins in Figure 2.5. Here the covalent bonding occurs by an SN2 reaction between a nucleophile, usually an amine, and a terminal epoxide. In the following example, the same bisphenol A intermediate used as a monomer for Lexan serves as a difunctional scaffold to which the epoxide rings are attached. Bisphenol A is prepared by the acid-catalyzed condensation of acetone with phenol [40].

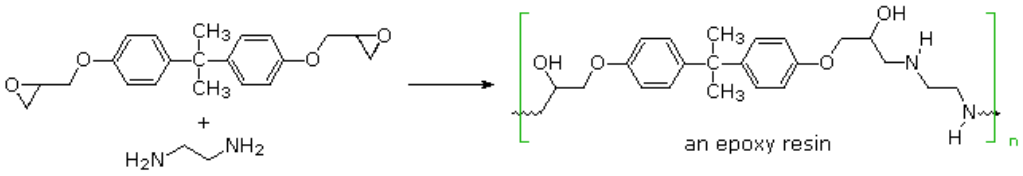


Figure 2.5: The structure of an epoxy resin.

2.2 Polyester Polyols

The polyester polyols are produced by the polycondensation of di- and polycarboxylic acids with an excess of polyfunctional alcohols. Building blocks for polyester polyols are presented in Table 2.1. The most important polycarboxylic acids and their anhydrides, which are available in industry, include aromatic acids (phthalic acid and isophthalic acid), aliphatic acids (adipic acid and maleic acid), cycloaliphatic acids (tetrahydrophthalic acid and hexahydrophthalic acid). Ethylene glycol, 1,2-propanediol, 1,6-hexanediol, neopentyl glycol, glycerol and trimethylolpropane,

cycloaliphatic alcohols such as 1,4-cyclohexanedimethanol are aliphatic alcohols which are used as polyols.

Polyester polyols are synthesized by a polycondensation reaction of polycarboxylic acids with polyols, splitting of water. There are two ways to synthesize; the first one is azeotropic esterification performed in an azeotropic organic solvent. Azeotropic solvent acts as the carrier to remove the water from the reaction medium. The second one is melt condensation process in which the coreactants are reacted in melt at temperatures at approximately 160-260°C. The reaction can be performed either in vacuum or in a stream of inert gas to remove the water from the medium.

The polyester polyols are suitable for broad range applications from vehicle finishing to general industrial coatings. Commercial polyester products have a molecular weight of 500 to 5000 Da. They can whether be liquid or solid, hard and soft resins depending on the chemical structure (Table 2.1) [41,42].

Table 2.1: Building blocks for polyester polyols.

Diol/Triol	Dicarboxylic Acid
Ethylene glycol	Adipic acid
1,2-Propane diol	Maleic acid
1,4-Butane diol	Phthalic acid
1,6-Hexane diol	Hexahydrophthalic acid
Neopentyl glycol	Isophthalic acid
Diethylene glycol	
Glycerol	
Trimethylol propane	

2.3 Click Chemistry

In 2001, Sharpless and coworkers introduced “click” chemistry, a new approach in organic synthesis that involves a collection of almost perfect chemical reactions. Sharpless describes click chemistry as tailored to generate substances quickly and reliably by joining small units together. Click chemistry can be summarized with only

one sentence: Molecules that are easy to make. Sharpless also introduced some criteria in order to fulfill the requirements of click reactions, which reactions are modular, wide in scope, high yielding, create only inoffensive by-products, reactions are stereospecific, simple to perform and that require benign or easily removed solvent [43].

Nowadays there are several processes have been identified under this term in order to meet these criteria. Nucleophilic ring opening reactions; non-aldol carbonyl chemistry; thiol additions to carbon–carbon multiple bonds (thiol-ene and thiol-yne); and cycloaddition reactions fulfill Sharpless's criteria (Figure 2.6) [44]. Among those selected reactions, copper (I)-catalyzed azide-alkyne (CuAAC), active ester reactions and Diels-Alder (DA) cycloaddition reactions have gained much interest among the chemists not only the synthetic ones but also the polymer chemists. From this point of view, these reactions will shortly be summarized.

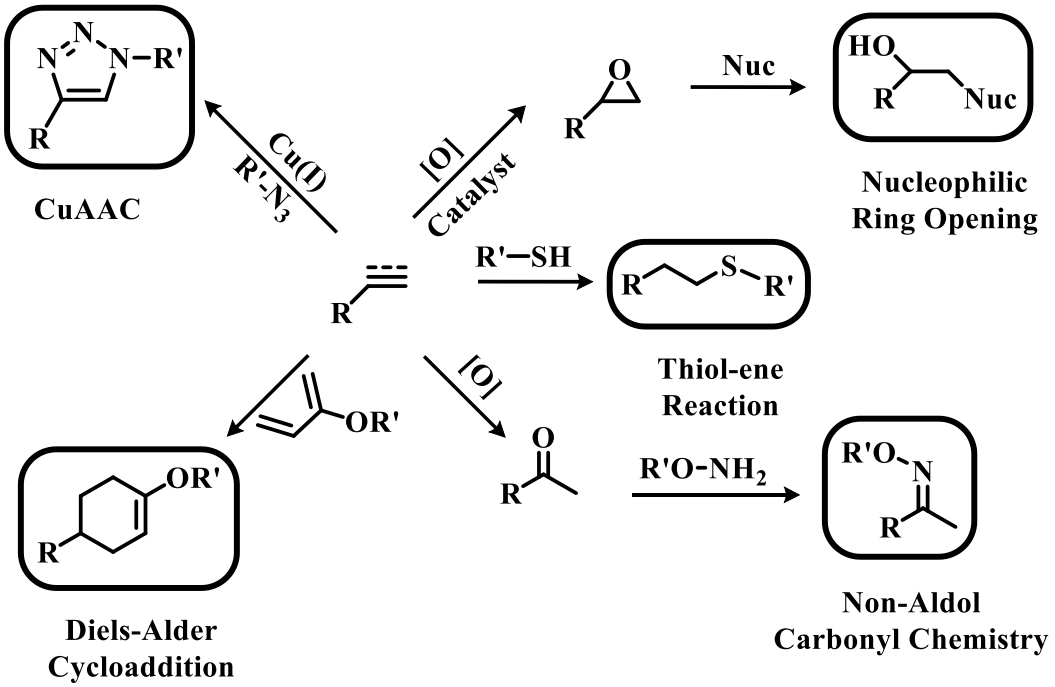


Figure 2.6: General representation of popular click reactions.

2.3.1 Copper (I) catalyzed azide-alkyne cycloaddition (CuAAC)

The thermal reaction between organic azides and alkynes has been known for more than a century, the first 1,2,3-triazole being synthesized by A. Michael from phenyl azide and diethyl acetylenedicarboxylate in 1893. The reaction has been investigated in detail by Huisgen and coworkers in the middle of the 20th century in the course of

their studies of the larger family of 1,3-dipolar cycloaddition reactions [45]. The Huisgen 1,3-dipolar cycloaddition reaction of alkynes and organic azides has gained considerable the most attention of any click reaction since 2001, CuAAC was realized independently by Fokin and Sharpless, and Meldal in 2002 [46,47]. The conventional Huisgen cycloaddition of azides and alkynes is not appropriate the criterion of a click reaction, because of the high temperature necessity (>110 °C) and the lack of regiospecificity which produce products with a racemic mixture of 1,4-triazole and 1,5-triazole products as seen in Figure 2.7 [45]. The copper catalyzed reaction allows to proceed much faster under much milder conditions and produces only one isomer which is 1,4-regiosomer triazole [43, 48]. The great success of the Cu (I) catalyzed reaction is actually a virtually quantitative, very robust, insensitive, general, and orthogonal ligation reaction.

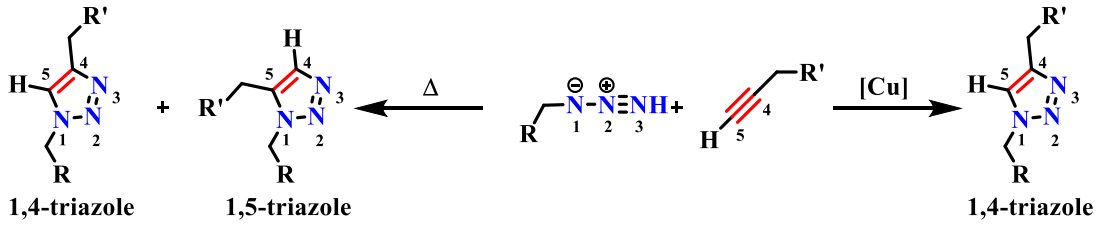


Figure 2.7: Huisgen's 1,3-dipolar cycloaddition and CuAAC.

When the mechanism is catalyzed, Cu (I) can easily overcome the activation barrier as a result of this difference the CuAAC reaction rate is increased by a factor of 10^7 relative to the Huisgen 1,3-dipolar cycloaddition, so it considerably fast at and below room temperature [49,50]. The reaction is not significantly affected by the steric and electronic properties of the functional groups attached to the azide and alkyne centers, and the CuAAC is fairly general with a broad range of alkynes and azides [51].

In fact, the discovery of Cu (I) as catalyst has a great importance which efficiently and regiospecifically combines terminal alkynes and azides under mild conditions. On the other hand, Fokin and Sharpless reported that only 1,5-disubstituted 1,2,3-triazole was obtained from terminal alkynes when the catalyst switched from Cu(I) to ruthenium(II) [52].

Although CuAAC reaction was initially postulated in general for organic synthesis, this strategy has also an enormous potential in polymer chemistry. The importance of CuAAC in polymer chemistry is the synthesis of functionalized polymers and the construction of polymers with well-defined architectures. Since the first report of click

chemistry in polymer science which is published by Hawker, Sharpless and coworkers, the construction of well-defined and complex macromolecular architectures via click chemistry has been used in many study and the number of publications in this field has increased dramatically within the years [53].

2.3.2 Diels-Alder Reaction

The Diels-Alder reaction (DA) is a concerned [4π+2π] cycloaddition reaction of a conjugated diene and a dienophile, 4 and 2 stand for the number of π electrons in the electronic rearrangement and the number of atoms of the unsaturated six-membered ring which is generated by the reaction of diene and dienophile. Reorganization of the π electrons, formation of two new sigma bonds and one new π bond all take place in a concerted manner as shown in Figure 2.8. Otto Diels and Kurt Alder discovered the Diels-Alder reaction in 1928, and the name of the reaction comes from their names; whom were awarded the Nobel Prize in 1950 [54,55].

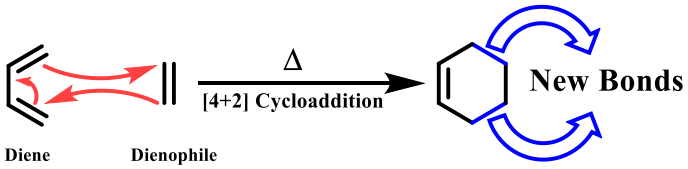


Figure 2.8: General mechanism of Diels-Alder reaction.

Some attractive features of DA reactions are that they are thermally reversible. The decomposition of the cyclic product, which is called as retro-Diels-Alder, can be controlled by temperature (Figure 2.9) [56].

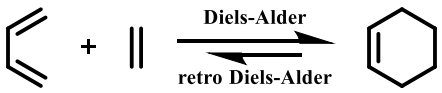


Figure 2.9: General mechanism of DA and retro DA.

Conjugated dienes and dienophiles can be used in a great variety for constructing many different simple and complex molecules. In a typical Diels-Alder reaction the diene is substituted with electron donating functional groups such as -OR, -NR_2 and the dienophile is substituted with electron withdrawing functional groups such as –COOR, -CN, -CO, -NO_2 and in this cases the reactivity of diene and dienophile increases [57].

2.3.3 Stereochemistry of Diels-Alder reaction

There are stereo chemical and electronic requirements for the DA reaction to occur smoothly. Even if an s-trans conformation is more stable than an s-cis conformation, the diene must be in s-cis conformation instead of s-trans conformation to allow maximum overlap of the orbitals, which are participating in the reaction (s stands for single bond) (Figure 2.10). Over time s-trans conformer is converted to s-cis conformer when reaction proceeds.

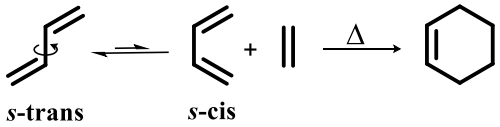


Figure 2.10: Conformation to interconversion during DA reaction.

When diene is a cyclic compound, DA reaction produce bridged bicyclic compounds. There are two different configuration for the product is possible, endo and exo products. The dienophile can line up in two different ways. The substituent on the dienophile can point either toward the large bridge (endo) or away from the large bridge (exo) as seen in Figure 2.11 and Figure 2.12.

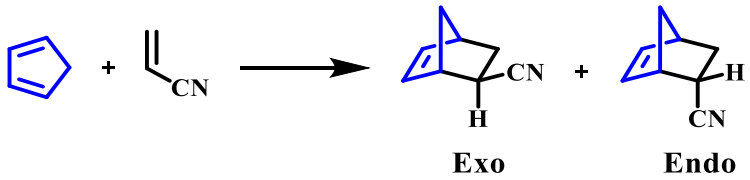
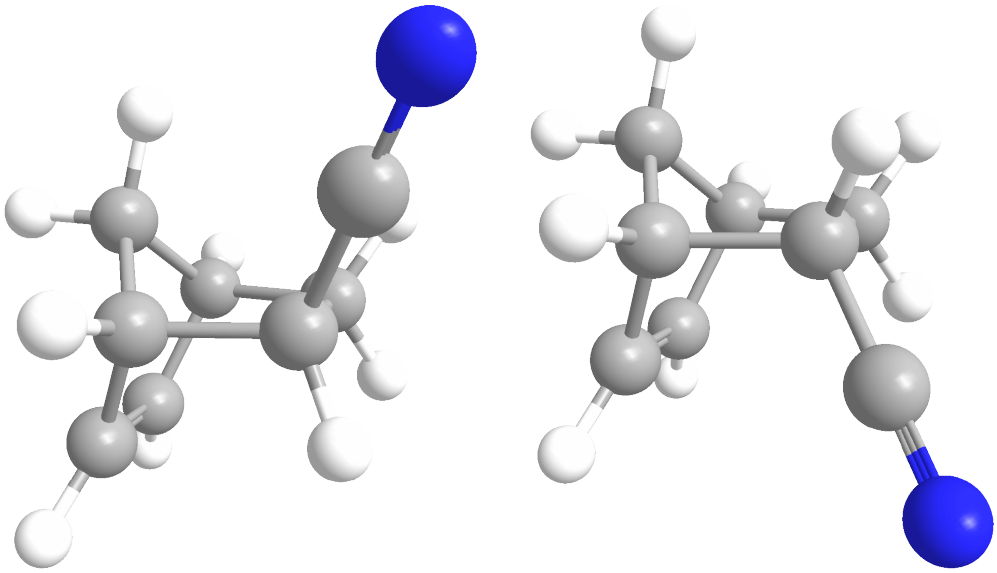


Figure 2.11: Endo and exo products of DA reaction.



Exo Isomer Endo Isomer

Figure 2.12: Stick-ball model of exo and endo products.

For instance, endo and exo products observed in most DA reactions, but the formation of endo product, which is more hindered product, puzzled the scientists. Woodward, Hoffmann, and Fukui used the molecular orbital theory to explain overlap of the p-orbitals on the substituents on the dienophile and with p-orbitals on the diene, which is favorable and helps to bring the two molecules together [58,59]. Hoffmann and Fukui shared the 1981 Nobel Prize in chemistry for their molecular orbital explanation of DA reaction and other organic reactions. Figure 2.13 shows orbital overlaps of possible products, one easily can notice the favorable overlap of the diene and the substituent on the dienophile in the formation of the endo product.

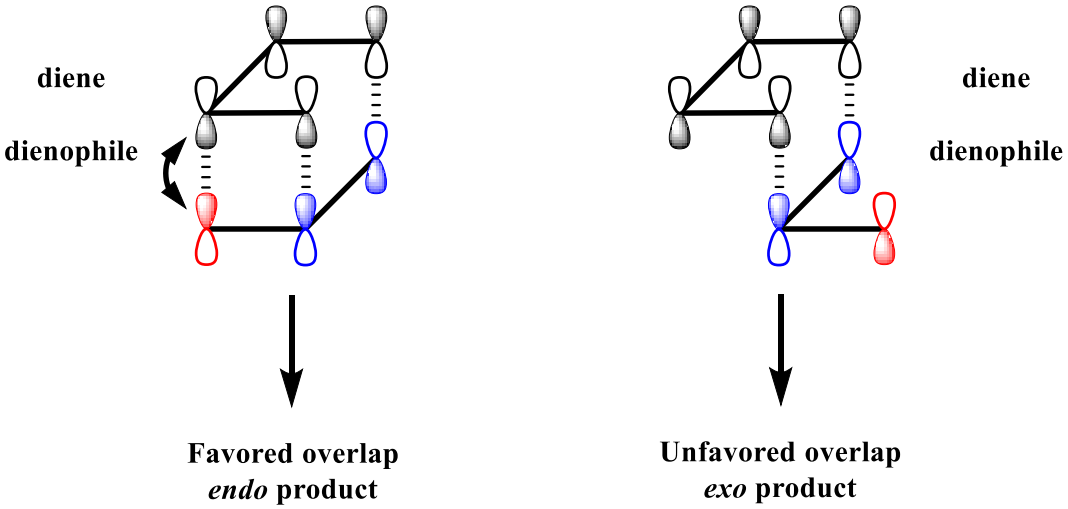


Figure 2.13: Molecular orbitals overlaps of possible products of DA reaction.

DA reaction is a reversible reaction at elevated temperatures, because of this reason the endo/exo ratio depends on the reaction temperature. Therefore, use of high temperatures and extended reaction times can result in the formation of the exo product, which is thermodynamically more favorable, at the expense of the endo product, which is the kinetic product.

2.4 1,3-Dipolar Cycloaddition Reaction

The Huisgen Cycloaddition is basically the reaction of a dipolarophile with a 1,3-dipolar compound that leads to 5-membered heterocycles. Examples of dipolarophiles are alkenes and alkynes and molecules that possess related heteroatom functional groups (such as carbonyls and nitriles). 1,3- Dipolar compounds contain one or more heteroatoms and can be described as having at least one mesomeric structure that represents a charged dipole [60].

This reaction is highly exothermic, but the high activation barrier is responsible for a very low reaction rate, even at elevated temperature. Another drawback is the formation of regioisomers, as the two possible HOMO-LUMO interactions of the substrates are closely related in terms of energy. The thermal reaction therefore often gives approximately 1:1 mixtures of both the 1,4-substituted and the 1,5-substituted regioisomers **(** Figure 2.14) [61].

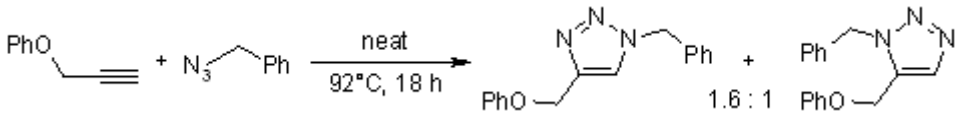


Figure 2.14: Mechanism of the Huisgen Azide-Alkyne 1,3-Dipolar Cycloaddition Reaction

In his seminal work, Rolf Huisgen defined 1,3-dipolar cycloadditions as "1,3 Dipole, a-b-c, must be defined, such that atom a posseses an electron sextet, that is, an incomplete valence shell combined with a positive formal charge, and that atom c, the negatively charged center, has an unshared electron pair. Combination of such a 1,3-dipole with a multiple bond system d-e, termed the dipolarophile, is referred to as a 1,3- dipolar cycloaddition." [62]. 1,3-Dipolar cycloaddition (1,3-DC) has become a fundamental organic reaction, and its high utility spreads in every aspect of chemistry, from natural product synthesis, material science, and chemical biology [63].

3. EXPERIMENTAL WORK

3.1 Materials

Tetrahydrofuran (THF, 99.8 %, J.T. Baker) was dried and distilled from benzophenone-sodium. Dichloromethane (CH2Cl2, 99%, J. T. Baker) was dried and distilled over and P2O5. Benzene (99%, Aldrich), diethyl ether (99.7%, Aldrich), methanol (99.8 %, Aldrich) were used without further purification. *p*-Toluenesulfonic acid monohydrate (PTSA 99 %, Aldrich), acetylenedicarboxylic acid (ADCA, 95 %, Aldrich), 1,4-butanediol (99 %, Aldrich), tetraethylene glycol (99 %, Aldrich), 1,4-benzenedimethanol (99 %, Aldrich), 1,4-cyclohexanedimethanol (99 %, Aldrich), furan (98 %, Aldrich), 2,3-dimethyl-1,3-butadiene (contains 100 ppm BHT as stabilizer, 98%, Aldrich), furan (98 %, Aldrich), anthracene (99 %, Aldrich), benzyl bromide (99.8%, Aldrich) and sodium azide (99.5%, Aldrich) were used as received. All other reagents were purchased from Aldrich and used as received without further purification.

3.2 Instrumentation

^{1}H (500 MHz) and ^{13}C (125 MHz) spectra were recorded using an Agilent VNMRS 500 instrument in $CDCl_3$. The conventional gel permeation chromatography (GPC) measurements were carried out with an Agilent instrument (Model 1100) with a pump, refractive index and UV detectors and four Waters Styragel columns (HR 5E, HR 4E, HR 3, HR 2), (4.6 mm internal diameter, 300 mm length, packed with 5 μm particles). The effective molecular weight ranges of columns were 2000–4,000,000, 50–100,000, 500–30,000, and 500–20,000 g/mol, respectively. THF was used as eluent at a flow rate of 0.3 mL/min at 30 ^{o}C and toluene was used as an internal standard. The molecular weights of the polymers were calculated on the basis of linear polystyrene (PS) standards (Polymer Laboratories).

3.3 Synthetic Procedures

3.3.1 Synthesis of Polyester, P1 Using ADCA and 1,4-Butanediol

ADCA (2.00 g, 17.5 mmol, 1 equiv) was dissolved in 40 mL of benzene and stirred under nitrogen. 1,4-Butanediol (1.58 g, 17.5 mmol, 1 equiv) and PTSA (0.33 g, 1.75 mmol, 0.1 equiv) were added to the solution in that order. The mixture was gradually heated in a round bottomed flask, with a Dean-Stark apparatus attached, in an oil bath set to 100 °C and stirred overnight. After that time, solvent was removed under reduced pressure, THF was added to the residue and finally precipitated in methanol. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The obtained polymer was dried overnight in a vacuum oven at 40 °C. ^{1}H NMR ($CDCl_3$, δ) 4.30 (bs, 4H, C=OOC*H*$_2$CH$_2$CH$_2$C*H*$_2$OC=O), 1.82 (bs, 4H, C=OOCH$_2$C*H*$_2$C*H*$_2$CH$_2$OC=O); ^{13}C NMR ($CDCl_3$, δ) 151.6, 74.7, 66.0, 30.8, 25.0.

3.3.2 Synthesis of Polyester, P2 Using ADCA and Tetraethylene Glycol

ADCA (1.0 g, 8.8 mmol, 1 equiv) was dissolved in 20 mL of benzene and stirred under nitrogen and tetraethylene glycol (1.51 mL, 8.80 mmol, 1 equiv) and PTSA (0.17 g, 0.90 mmol, 0.1 equiv) were added to the solution in that order. The mixture was gradually heated in a round bottomed flask, with a Dean-Stark apparatus attached, in an oil bath set to 100 °C and stirred overnight. After that time, solvent was removed under reduced pressure, THF was added to the residue and finally precipitated in methanol. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The obtained polymer was dried overnight in a vacuum oven at 40 °C. ^{1}H NMR ($CDCl_3$, δ) 4.40 (m, 4H, C=OOC*H*$_2$CH$_2$O), 3.75 (m, 4H, C=OOCH$_2$C*H*$_2$O), 3.67 (s, 8H, OC*H*$_2$C*H*$_2$O); ^{13}C NMR ($CDCl_3$, δ) 151.7, 74.9, 70.6, 68.4, 65.8.

3.3.3 Synthesis of Polyester, P3 Using ADCA and 1,4-Benzenedimethanol

ADCA (0.50 g, 4.4 mmol, 1 equiv) was dissolved in 20 mL of benzene and stirred under nitrogen. 1,4-Benzenedimethanol (0.60 g, 4.4 mmol, 1 equiv) and PTSA (0.08 g, 0.4 mmol, 0.1 equiv) were added to the solution in that order. The mixture was gradually heated in a round bottomed flask, with a Dean-Stark apparatus attached, in an oil bath set to 100°C and stirred overnight. After that time, solvent was removed under reduced pressure, THF was added to the residue and finally precipitated in methanol. The dissolution–precipitation (THF-methanol) procedure was repeated two

times. The obtained polymer was dried overnight in a vacuum oven at 40 °C. ^{1}H NMR ($CDCl_3$, δ) 7.38 (bs, 4H, Ar*H*), 5.25 (bs, 4H, C=OOC*H*$_2$Ph), 4.57 (s, 4H, C=OOC*H*$_2$Ph); ^{13}C NMR ($CDCl_3$, δ) 151.2, 134.7, 129.2, 128.9, 128.0, 126.2, 74.8, 71.6, 68.3, 41.6

3.3.4 Synthesis of Polyester, P4 Using ADCA and 1,4-Cyclohexanedimethanol

ADCA (1.0 g, 8.8 mmol, 1 equiv) was dissolved in 20 mL of benzene and stirred under nitrogen and 1,4-cyclohexanedimethanol (1.26 g, 8.80 mmol, 1equiv) and PTSA (0.17 g, 0.90 mmol, 0.1 equiv) were added to the solution in that order. The mixture was gradually heated in a round bottomed flask, with a Dean-Stark apparatus attached, in an oil bath set to 100 °C and stirred overnight. After that time, solvent was removed under reduced pressure, THF was added to the residue and finally precipitated in methanol. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The obtained polymer was dried overnight in a vacuum oven at 40 °C. ^{1}H NMR ($CDCl_3$, δ) 4.16 (m, 4H, C*H*$_2$CH), 4.08 (m, 4H, C*H*$_2$CH), 2.1-1.0 (m, aliphatic protons of cyclohexane); ^{13}C NMR ($CDCl_3$, δ) 151.9, 74.8, 71.5, 69.4, 36.6, 34.1, 28.4, 25.0.

3.3.5 Diels-Alder Cycloaddition Reaction Between P1 and Furan (P5)

P1 (0.1 g, 0.6 mmol of alkyne, 1 equiv) was dissolved in 3 mL of 1,4-dioxane and transferred to a 10 mL of Schlenk tube. Next furan (86.6 µL, 1.20 mmol per alkyne, 2 equiv) was added to the solution and the reaction mixture was degassed by two FPT cycles, left in vacuum and stirred for 16 h at 100 °C. After the specified time, solution was precipitated in methanol and residual solvent was removed by decantation. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The recovered polymer was dried in a vacuum oven at 40 °C for 24 h (Yield = 0.10 g, 71 %, $M_{n,GPC}$ = 6200 g/mol, M_w/M_n = 1.68, relative to PS standards). ^{1}H NMR ($CDCl_3$, δ) 7.23 (s, 2H, C*H*=C*H*), 5.68 (s, 2H, C*H*O, bridge-head protons), 4.25 (bs, 4H, C=OOC*H*$_2$CH$_2$CH$_2$C*H*$_2$OC=O), 1.80 (bs, 4H, C=OOCH$_2$C*H*$_2$C*H*$_2$CH$_2$OC=O); ^{13}C NMR ($CDCl_3$, δ) 162.6, 153.1, 151.7, 143.2, 851, 73.2, 66.3, 65.9, 64.8, 29.7, 25.1.

3.3.6 Diels-Alder Cycloaddition Reaction Between P1 and 2,3-Dimethyl-1,3-Butadiene (P6)

P1 (0.1 g, 0.6 mmol of alkyne, 1 equiv) was dissolved in 3 mL of 1,4-dioxane and transferred to a 10 mL of Schlenk tube. Next 2,3-Dimethyl-1,3-Butadiene (134.7 µL,

1.2 mmol per alkyne, 2 equiv) was added to the solution and the reaction mixture was degassed by two FPT cycles, left in vacuum and stirred for 16 h at 80 °C. After the specified time, solution was precipitated in methanol and residual solvent was removed by decantation. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The recovered polymer was dried in a vacuum oven at 40 °C for 24 h (Yield = 0.08 g, 54 %, $M_{n,GPC}$ = 6700 g/mol, M_w/M_n = 1.75, relative to PS standards). ^{1}H NMR ($CDCl_3$, δ) 4.20 (bs, 4H, C=OOC*H*$_2$CH$_2$CH$_2$C*H*$_2$OC=O), 2.91 (bs, 4H, C=CC*H*$_2$C=C), 1.76 (bs, 6H, C*H*$_3$), 1.67 (bs, 4H, C=OOCH$_2$C*H*$_2$C*H*$_2$CH$_2$OC=O); ^{13}C NMR ($CDCl_3$, δ) 167.9, 132.8, 130.0, 121.5, 64.5, 34.2, 25.2, 19.7, 18.0.

3.3.7 Diels-Alder Cycloaddition Reaction Between P1 and Anthracene (P7)

P1 (0.10 g, 0.6 mmol of alkyne, 1 equiv) was dissolved in 3 mL of 1,4-dioxane and transferred to a 10 mL of Schlenk tube. Next anthracene (0.21 g, 1.2 mmol per alkyne, 2 equiv) and 2 mL of DMF were added to the solution. The reaction mixture was degassed by two FPT cycles, left in vacuum and stirred for 16 h at 120 °C. After the specified time, solution was precipitated in methanol and residual solvent was removed by decantation. The dissolution–precipitation (THF-methanol) procedure was repeated two times. The recovered polymer was dried in a vacuum oven at 40 °C for 24 h (Yield = 0.13 g, 63 %, $M_{n,GPC}$ = 5750 g/mol, M_w/M_n = 1.44, relative to PS standards). ^{1}H NMR ($CDCl_3$, δ) 7.37 (bs, 2H, Ar*H*), 7.00 (bs, 2H, Ar*H*), 5.46 (bs, 2H, C*H*, bridge protons), 4.16 (bs, 4H, C=OOC*H*$_2$CH$_2$CH$_2$C*H*$_2$OC=O), 1.70 (bs, 4H, C=OOCH$_2$C*H*$_2$C*H*$_2$CH$_2$OC=O); ^{13}C NMR ($CDCl_3$, δ) 165.3, 151.7, 146.9, 143.7, 125.4, 123.8, 74.9, 66.3, 65.6, 64.8, 64.6, 52.5, 25.0, 24.9.

3.3.8 Synthesis of Benzyl Azide

To a stirred solution of the benzyl bromide (0.4276 g, 2.5 mmol) in a 50 mL water/acetone mixture (1:4) was added NaN3 (0.244 g, 3.75 mmol).The resulting suspension was stirred at 60°C for 24 hours. DCM was added to the mixture and the organic layer was separated. The aqueous layer was extracted with 3 x 10 mL aliquots of DCM and the combined organic layers were dried over Na2SO4. Solvent was removed under reduced pressure and 5 afforded as colorless oil (Yield=0.3 g, 90%). 1H NMR (CDCl3, δ) 7.32-7.43 (m, 5H, aromatic protons), 4.35 (s, 2H CH2-N3).

3.3.9 Functionalization of P5 via Sequential 1,3-Dipolar Cycloaddition/retro-Diels-Alder Reactions (P8)

P8 (0.10 g, 0.42 mmol, 1 equiv) and benzyl azide (0.11 g, 0.84 mmol, 2 equiv) and 3 mL of THF were added in a 10 mL flask. The reaction mixture was stirred at room temperature under nitrogen overnight and after that time, precipitated in methanol. The dissolution–precipitation (THF-methanol) procedure was repeated two times and the recovered polymer, **P11** was dried in a vacuum oven at 40 ^{o}C for 24 h (Yield = 0.07 g, 45 %, $M_{n,GPC}$ = 6700 g/mol, M_w/M_n = 1.53, relative to PS standards). ^{1}H NMR ($CDCl_3$, δ) 7.31 (m, Ar*H*), 5.78 (bs, 2H, CH_2Ph), 4.30 (m, 4H, C=OOCH_2CH$_2$CH$_2$CH_2OC=O), 1.80 (m, 4H, C=OOCH$_2$CH_2CH_2CH$_2$OC=O); ^{13}C NMR ($CDCl_3$, δ) 161.4, 160.0, 158.4, 148.4, 140.1, 134.0, 130.1, 128.8, 129.9, 127.9, 118.3, 66.2, 65.9, 65.2, 65.0, 64.1, 53.8, 29.7, 25.2, 24.9, 24.6.

4. RESULTS AND DISCUSSION

4.1 Preparation of Polyesters

Polyesterification reactions were performed under standard conditions using ADCA and readily available various diols in the presence of catalytic amount of PTSA in benzene at 100 ^{o}C overnight.

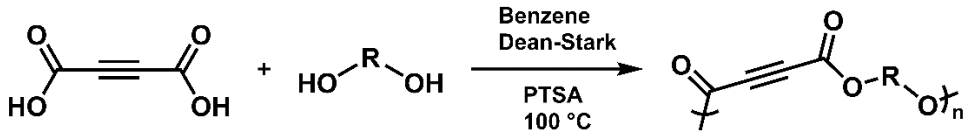


Figure 4.1: General Synthetic Procedure of Polyesters.

ADCA, the diol compound and PTSA was suspended in benzene then gradually heated in a round bottomed flask, with a Dean-Stark apparatus attached, in an oil bath set to 100 °C and stirred overnight. After the dissolution-precicpitation, the recovered polymer was dried overnight in a vacuum oven at 40 ^{o}C, obtained as a grey powder.

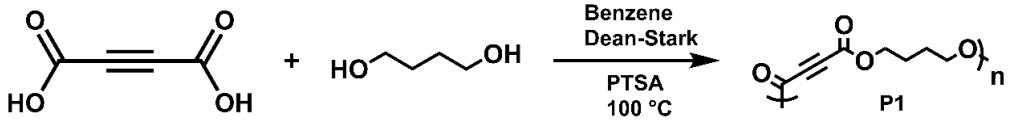


Figure 4.2: Synthesis of **P1**, using ADCA and Butanediol.

The reaction of **P1** was obtained via condensation polymerization by using butanediol as a diol within general procedure. The ^{13}C NMR spectra are informative for elucidating the structures of the polyesters while displaying signals at around 151.6 and 74.5 ppm assignable to the C=O and C≡C groups, respectively. ^{1}H NMR spectrum shows that the *OCH2* protons of polyester backbone and they appeared at 4.40 and 1.82 ppm after polymerizaiton.

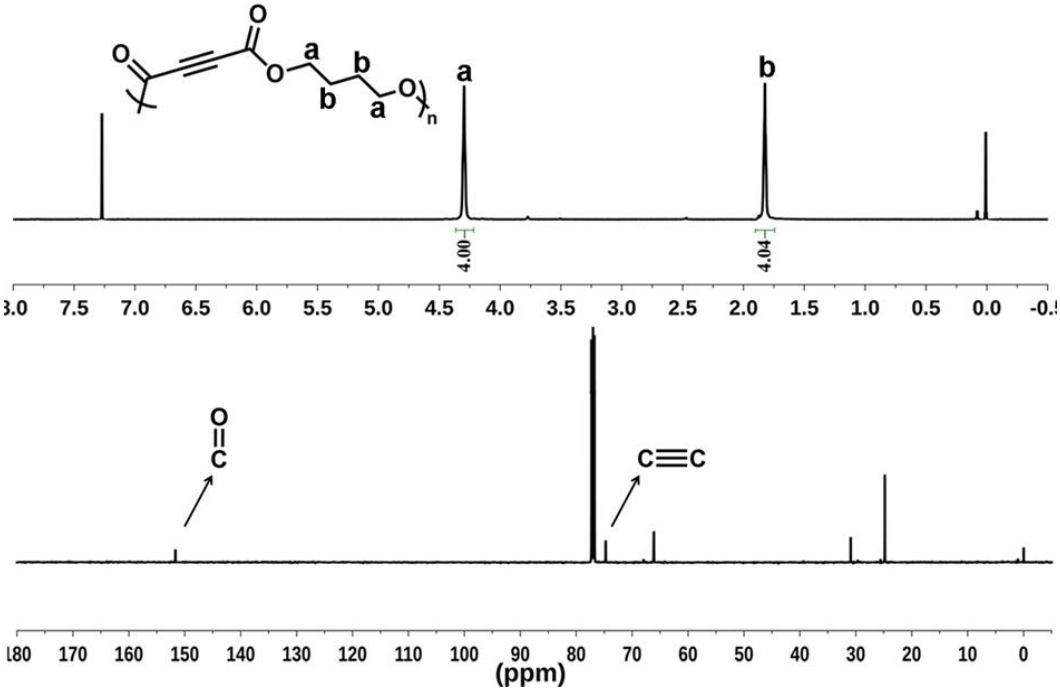


Figure 4.3: ^{1}H (up) and ^{13}C NMR (down) spectra of **P**1 in $CDCl_3$ (500 and 125 MHz, respectively).

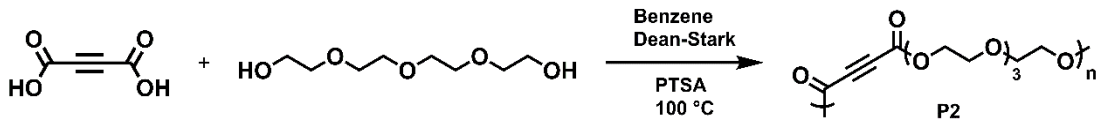


Figure 4.4: Synthesis of **P2**, using ADCA and Benzenedimethanol.

The reaction mechanism of **P2** is entirely the same as general polyester synthetic procedure with exception of using different diol, for this reaction tetraethyleneglycol was used as a diol. The ^{1}H NMR spectrum for the polyester **P2**, indicated that the protons next to the ester units (C=OOCH_2CH$_2$O) were detected at 4.40 ppm, the methylene groups (C=OOCH$_2$CH_2O) at 3.75 ppm and the protons of the tetraethylene's interior ethylene groups (OCH_2CH_2O) at 3.67 ppm, respectively. From the ^{13}C NMR spectrum, the peaks of 151.7 and 74.9 ppm are assigned C=O and C≡C groups and the peaks in the range of between 70.6 and 65.8 ppm are identified to ethylene groups carbons.

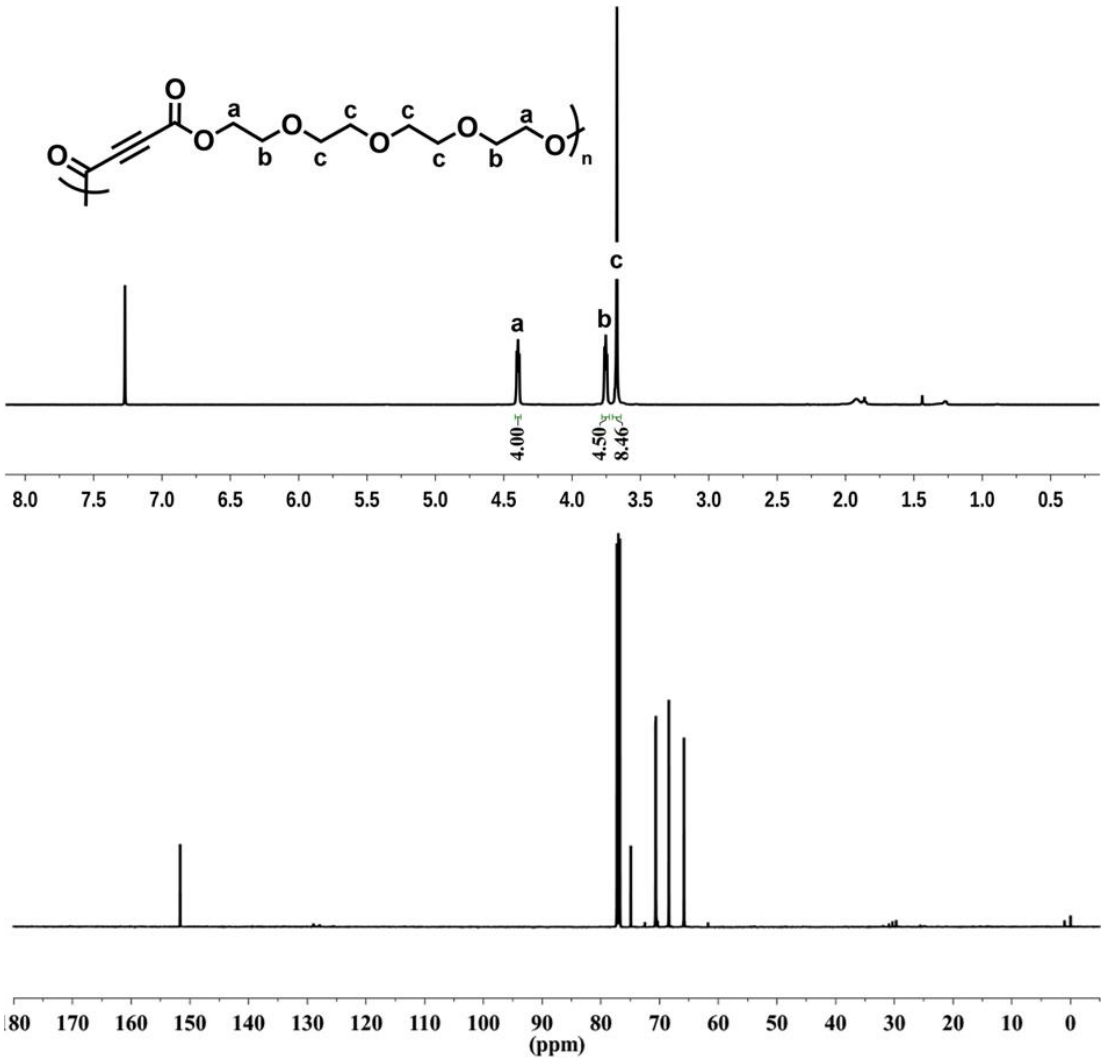


Figure 4.5: ^{1}H (up) and ^{13}C NMR (down) spectra of **P2** in $CDCl_3$ (500 and 125 MHz, respectively).

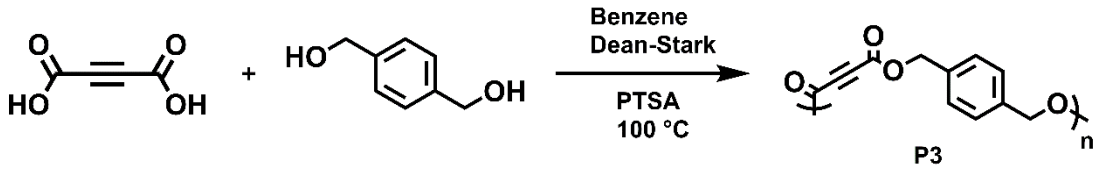


Figure 4.6: Synthesis of **P3**, using ADCA and Benzenedimethanol.

The reaction mechanism of **P3** is entirely the same as general polyester synthetic procedure with exception of using different diol, for this reaction benzenedimethanol was used as a diol. From the ^{1}H NMR spectrum for the polyester **P3,** indicated that the protons which Ar*H* of benzene at 7.38 ppm, next to the ester unit protons (C=OOCH_2Ph) were detected in the range of between at 5.25 and 4.57 ppm and the methylene groups (C=OOCH$_2$CH_2O) at 3.75 ppm. From the ^{13}C NMR spectrum, the

peaks of 151.2 and 74.8 ppm are assigned C=O and C≡C groups, respectively and the peaks in the range of between 134.7 and 41.6 ppm are identified to belonging carbons of benzenedimethanol.

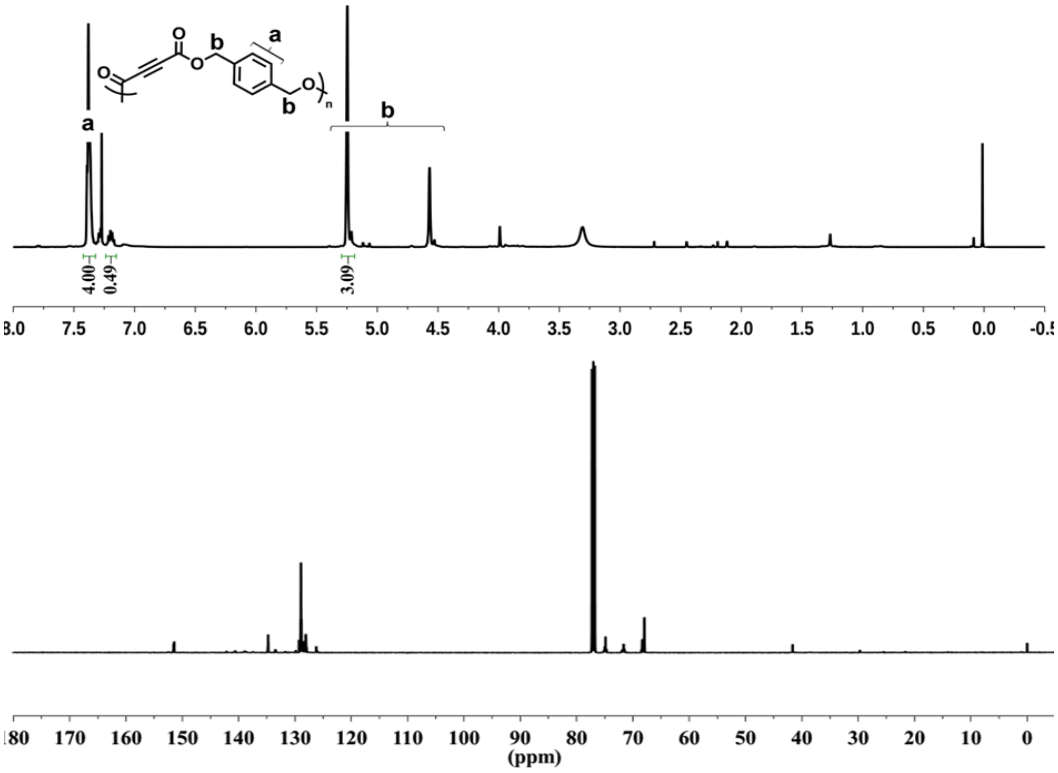


Figure 4.7: ^{1}H (up) and ^{13}C NMR (down) spectra of **P3** in $CDCl_3$ (500 and 125 MHz, respectively).

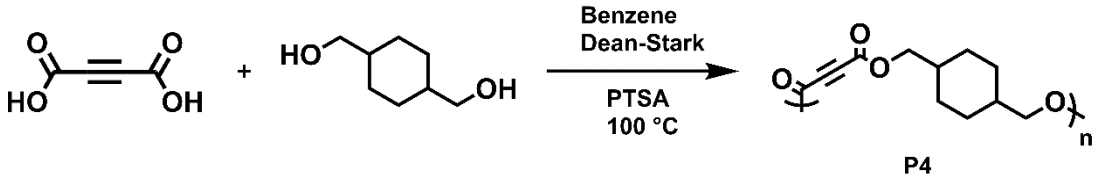


Figure 4.8: Synthesis of **P**4, using ADCA and Cyclohexanedimethanol.

The reaction mechanism of **P4** is entirely the same as general polyester synthetic procedure with exception of using different diol, for this reaction cyclohexanedimethanol was used as a diol. From the ^{1}H NMR spectrum for the polyester **P4**, indicated that next to the ester unit protons (C*H*$_2$CH) in the range of between at 4.16 and 4.08 ppm and the aliphatic protons of cyclohexane in the range of between at 2.1-1.0 ppm. From the ^{13}C NMR spectrum, the peaks of 151.9 and 74.8 ppm are assigned C=O and C≡C groups and the peaks in the range of between 71.5 and 25.0 ppm are identified to belonging carbons of cyclohexanedimethanol.

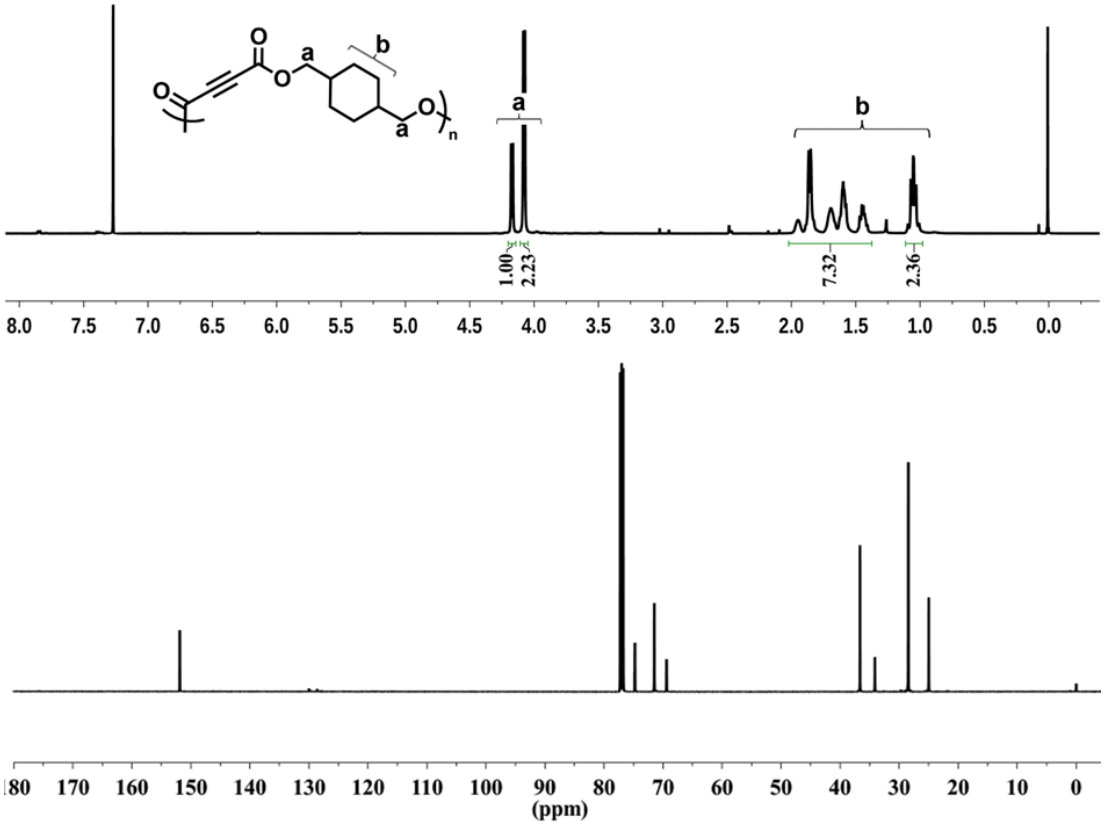


Figure 4.9: ^{1}H (up) and ^{13}C NMR (down) spectra of **P4** in $CDCl_3$ (500 and 125 MHz, respectively).

The GPC traces of all polyesters exhibited monomodal distributions, moderately high to low molecular weights (M_w of 46150 to 3850 g/mol) and high polydispersity index in the range of 3.00-1.62 (Table 4.1).

Table 4.1: Characteristic properties of polyesters from ADCA and various diols.

Polymer structure	Yield[a] (%)	$M_{n,GPC}$[b] (g/mol)	$M_{w,GPC}$[b] (g/mol)	M_w/M_n[b]
P1[c]	83	5070	8230	1.62
P2[d]	78	8650	15950	1.85
P3[e]	64	2100	3850	1.80
P4[f]	71	15350	46150	3.00

[a]Isolated yield; [b]GPC calibrated on the basis of linear PS standards in THF at 30 °C. [c]Butanediol backbone, [d]Tetraethylene backbone, [e]Benzenedimethanol backbone, [f]Cyclohexanedimethanol backbone.

4.2 Modification of Polyester via Diels-Alder Cycloaddition Reaction

In the second part of the study, modification of **P1** via Diels-Alder Cycloaddition reaction was carried out. Cycloaddition reaction ability of different diene compounds (2 equiv; furan, 2,3-dimethyl-1,3-butadiene and anthracene) were reacted with **P1** (1 equiv) through Diels-Alder reaction, in 1,4-dioxane at predetermined temperatures for 16 h.

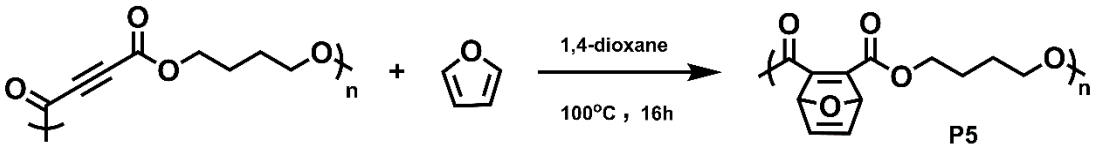


Figure 4.10: Synthesis of **P5** via Diels-Alder Cycloaddition Reaction

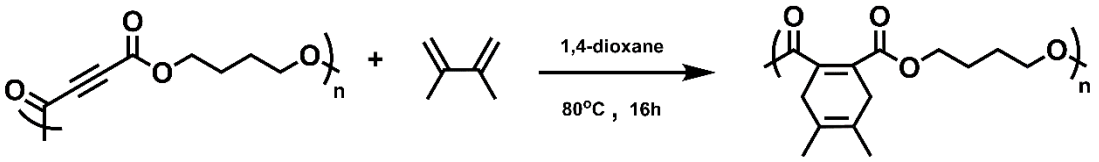


Figure 4.11: Synthesis of **P6** via Diels-Alder Cycloaddition Reaction

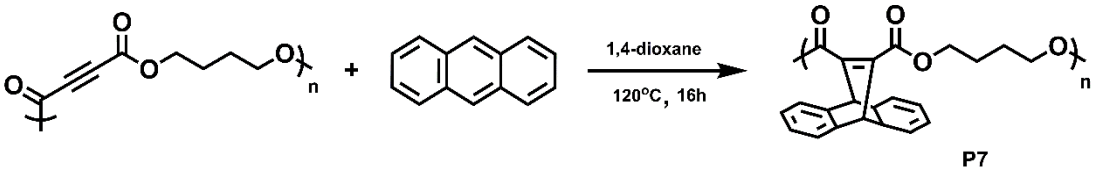


Figure 4.12: Synthesis of **P7** via Diels-Alder Cycloaddition Reaction

The 1H NMR spectra of the **P5**, **P6** and **P7** are shown in Figure 4.13. From the NMR spectra, the peaks in the range between 4.25 and 1.67 ppm (C=OOCH_2CH$_2$CH$_2$CH_2OC=O, C=OOCH$_2$CH_2CH_2CH$_2$OC=O) are assigned to methylene protons of the backbone for all the modificated polymers, respectively. The characteristic protons of the adduct belong to **P5,** were detected at 7.23 ppm (C*H*=C*H* , bridge vinyl protons) and 5.68 ppm (C*H*O, bridge-head protons). The 1H NMR spectrum result for **P6**, metylene group protons were detected at 2.91 ppm (C=CCH_2C=C) and methyl group protons 1.76 ppm. From the 1H NMR spectrum for

P7, the characteristic protons beloning to anthracene was detected at 7.37 ppm (Ar*H*), 7.00 ppm (Ar*H*) and 5.46 ppm (C*H*, bridge protons).

Moreover, From 1H NMR spectroscopy the Diels Alder reaction efficiencies were achieved by comparing the integrated characteristic signals of adduct structures and the OCH2 of polyester backbone (Figure 4.13). The polyester, **P1**, derived from ADCA and 1,4-butanediol was used as a model polymer during the course of the study due to its ease of handling and easy monitoring by NMR.

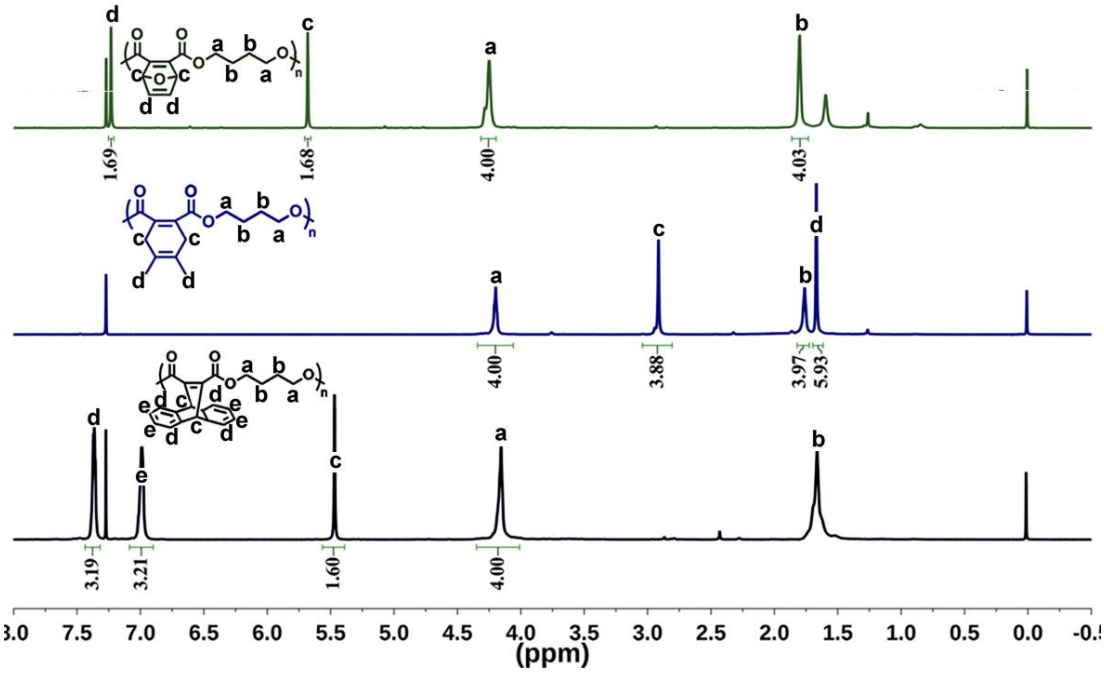


Figure 4.13: ^{1}H NMR spectra of **P5** (top), **P6** and **P7** (down) in $CDCl_3$ (500 MHz).

^{13}C NMR spectra results of all sythesized polymers confirmed their structure and clearly seen that the furan, 2,3-dimethyl-1,3-butadiene and anthracene-containing polymers were sucsessfully obtained.

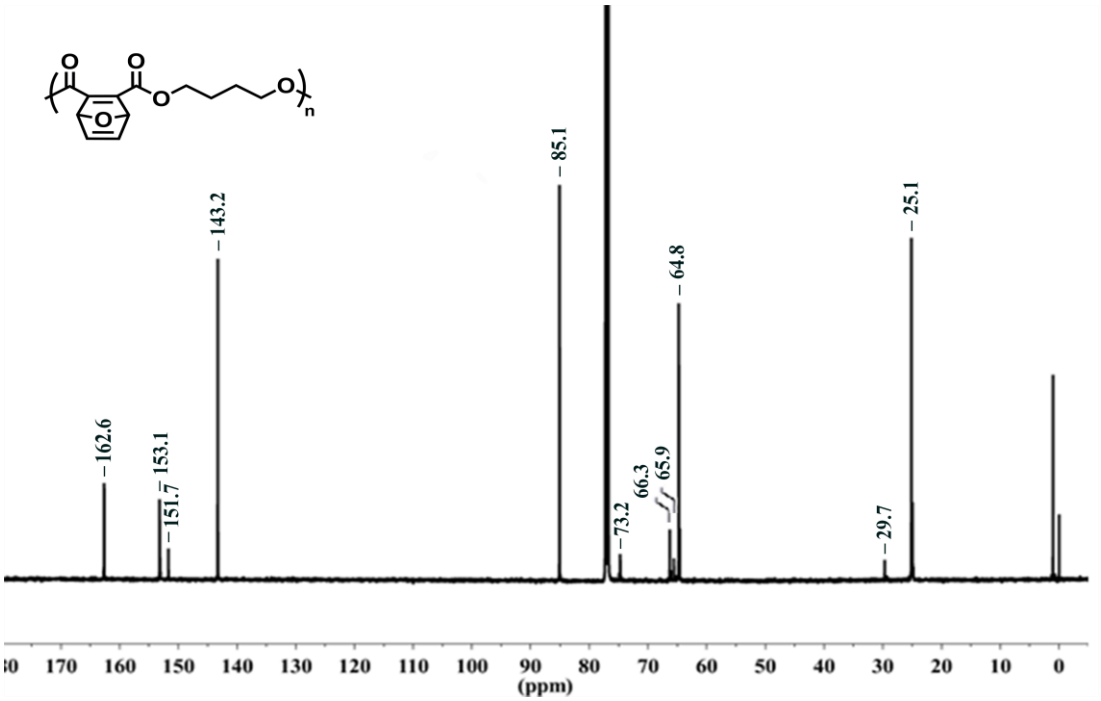


Figure 4.14: ^{13}C NMR spectrum of **P5** in $CDCl_3$ (125 MHz).

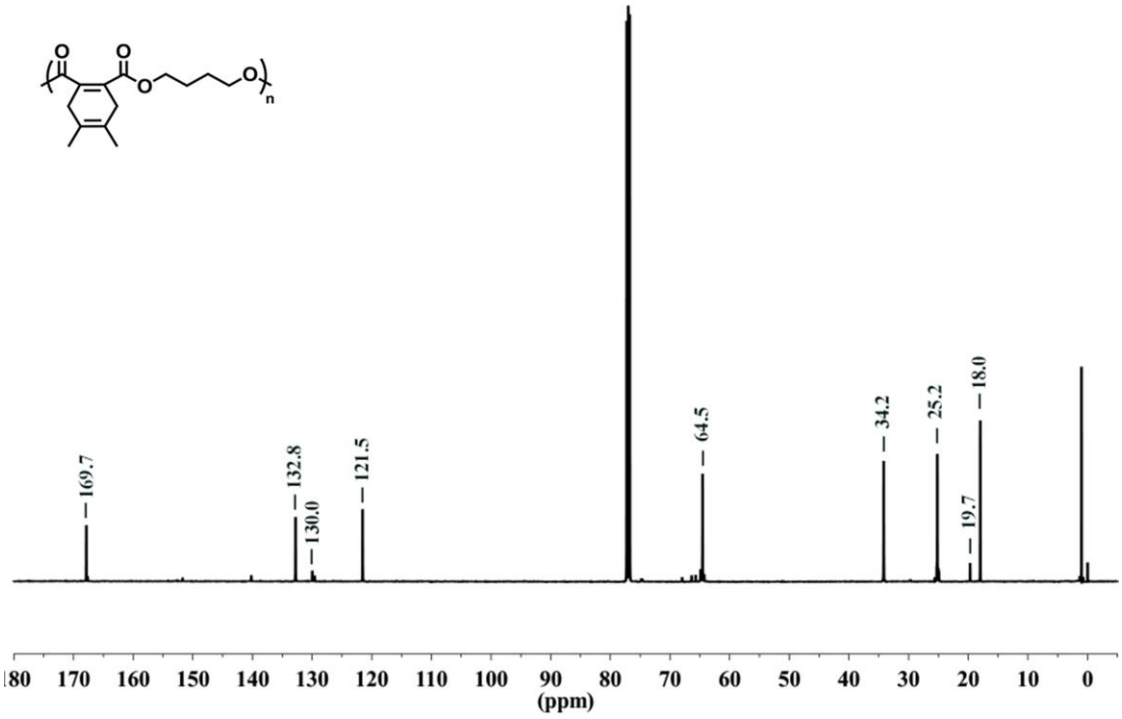


Figure 4.15: ^{13}C NMR spectrum of **P6** in $CDCl_3$ (125 MHz).

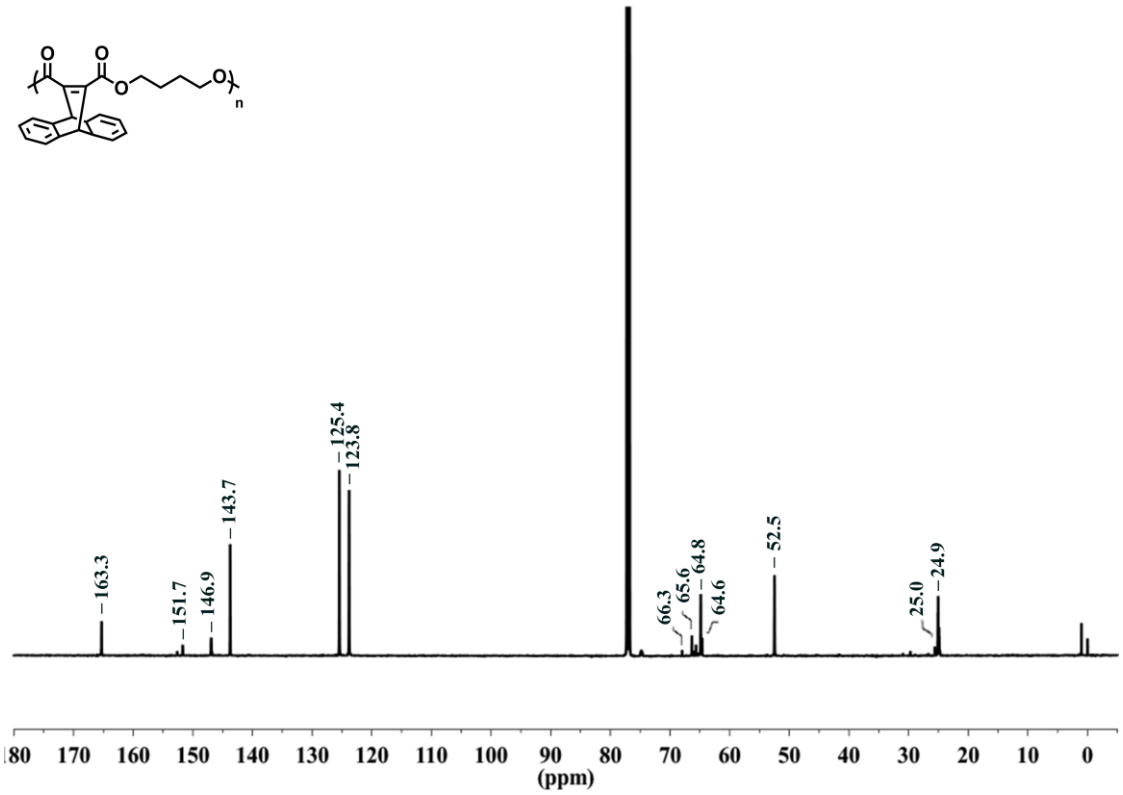


Figure 4.16: ^{13}C NMR spectrum of **P7** in $CDCl_3$ (125 MHz).

Moreover, the GPC traces of all polyesters exhibited monomodal distributions, moderately high to low molecular weights (M_w of 46150 to 3850 g/mol) and mild polydispersity index in the range of 1.75-1.44 (Table 4.2).

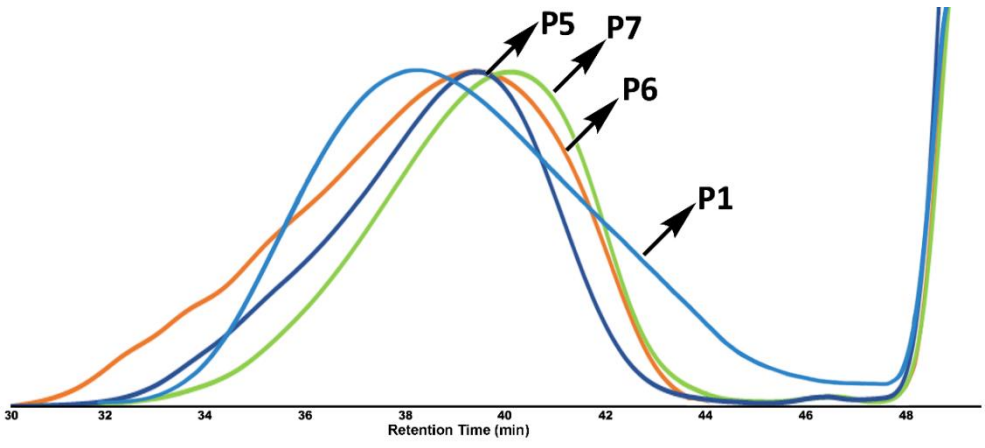
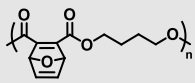
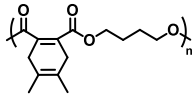
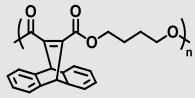


Figure 4.17: Overlay of GPC traces of compounds **P1, P5, P6** and **P7** in THF at 30°C.

Table 4.2: Characterization of polyesters after Diels-Alder cycloaddition reactions (**P1** and various dienes) in 1,4-dioxane for 16 h.

Polymer Structure	Temperature (°C)	*eff.*[a] (%)	$M_{n,GPC}$[b] (g/mol)	$M_{w,GPC}$[b] (g/mol)	M_w/M_n[b]
 **P5**	60	45	6200	10440	1.68
	80	83/84[c]			
	100	84/84[c]			
	110	75			
 **P6**	60	68	6700	11750	1.75
	80	97			
 **P7**	110	67	5750	8250	1.44
	120	78/80[c]			

[a]Calculated on the basis of integral ratios; [b]GPC calibrated on the basis of linear PS standards in THF at 30 °C; [c]Three equiv of dienes were used.

4.3 Preparetion of Benzyl Azide

Benzyl bromide converted to benzyl azide in water/acetone (1:4) mixture using NaN_3. Reaction mixture was stirred for 24 h at 60°C and compound 5 afforded as colorless oil (Figure 4.18).

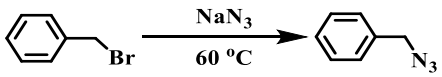


Figure 4.18: Synthesis of benzyl azide.

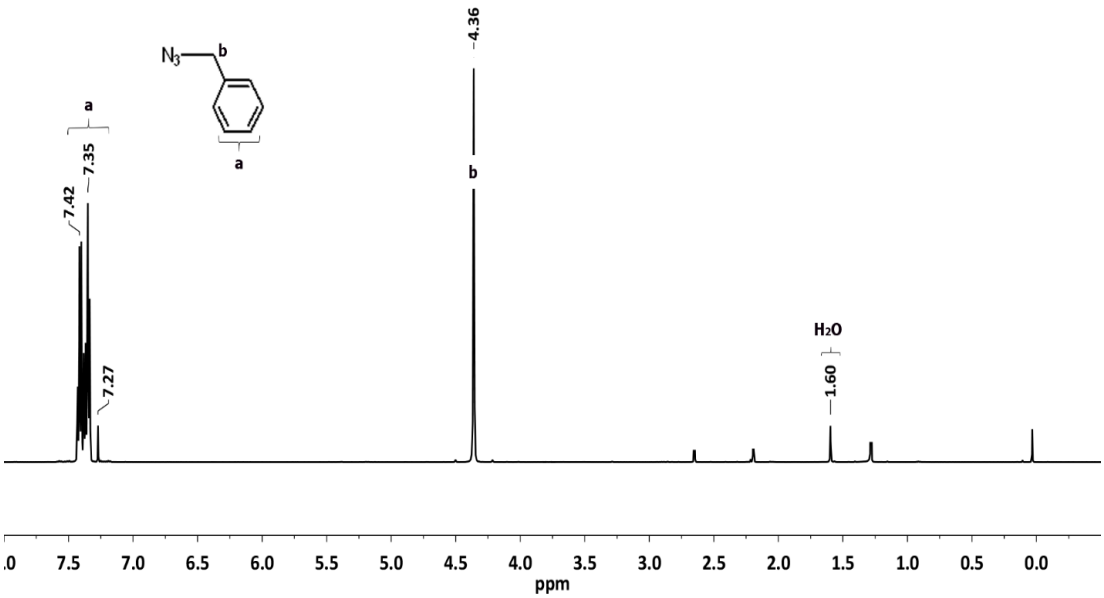


Figure 4.19: ^{1}H NMR spectrum of Benzyl Azide in $CDCl_3$ (500 MHz).

From ^{1}H NMR spectra of benzyl azide, it was clearly seen that aromatic protons of benzyl detected between 7.42-7.35 ppm, methylene next to azide found at 4.36 ppm, and integrated values of this signals validated the number of protons on the molecule (Figure 4.19).

4.4 Functionalization of Substitute Polyester via Sequential 1,3-Dipolar Cycloaddition/retro-Diels-Alder Reactions

In the case of the Diels-Alder cycloaddition reaction, temperature is crucial as can be seen from Table 4.2. It is clear that the higher cycloaddition reaction efficiencies are achieved at higher reaction temperatures. However, during the reaction of furan with **P1** in order to yield **P5**, the reaction efficiencies gradually increased with increasing temperature, and reached to a plateau at 80-100 ^{o}C (84% efficiency), then followed by a decrease over 100 ^{o}C in which the retro-Diels-Alder reaction is expected to be favored. Yet, efficiencies were still not affected even when 3 equiv of dienes relative to 1 equiv of alkyne was used. The cycloaddition reaction efficiencies did not measurably affect the molecular weights and polydispersity index of the resulting polyesters. Interestingly, an anthracene-adduct polyester, **P7**, displays a lower molecular weight and a polydispersity index than the pristine polymer, **P1**.

Among the Diels-Alder adducts, the furan-adduct polyester, **P5** has an oxanorbornadiene functionality that can undergo further sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reaction. As seen from Figure 4.21, an

oxanorbornadiene structure having two electron withdrawing groups (C=O) is reacted with benzyl azide in which it is attached to the double bond between two carbonyl groups, rather than to the less hindered double bonds. After that attack, a rearrangement occurs to produce the final product, while furan being removed. This effective chemistry is for the first time described by Cornellisen group in the bioconjugation of an electron deficient oxanorbornadiene-end functional polyethylene glycol with an azide-functionalized peptide [64].

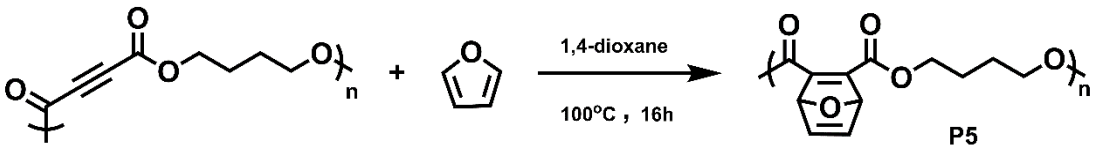


Figure 4.20: Synthesis of **P5**, to use for second part of the sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reaction.

Thus, we performed this reaction by using a 1 equiv of **P5** and a 2 equiv of benzyl azide in THF at room temperature overnight. The progress of the sequential reactions is monitored by NMR spectroscopy. From ^{1}H NMR, a signal related to bridge-head protons of furan adduct at 5.68 ppm disappeared and a new signal of CH_2Ph at 5.78 ppm appeared demonstrating that furan was completely removed while triazole ring formed simultaneously to yield the final structure (Figure 4.21).

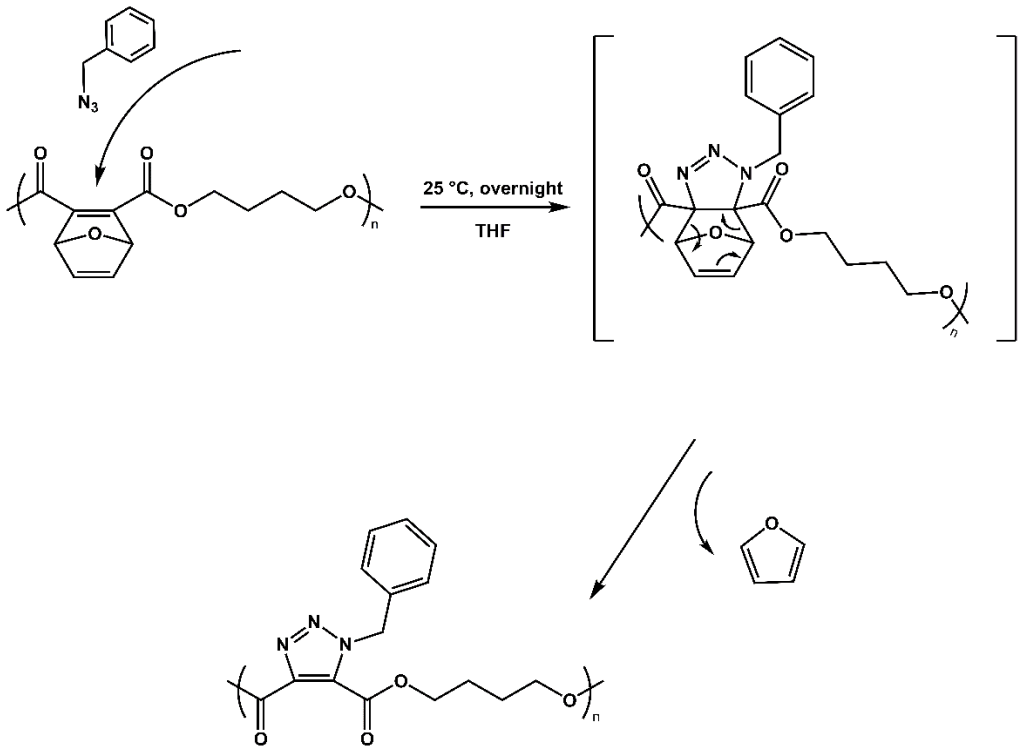


Figure 4.21: Sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reaction of **P5** in THF at 25°C overnight, Synthesis of **P8**.

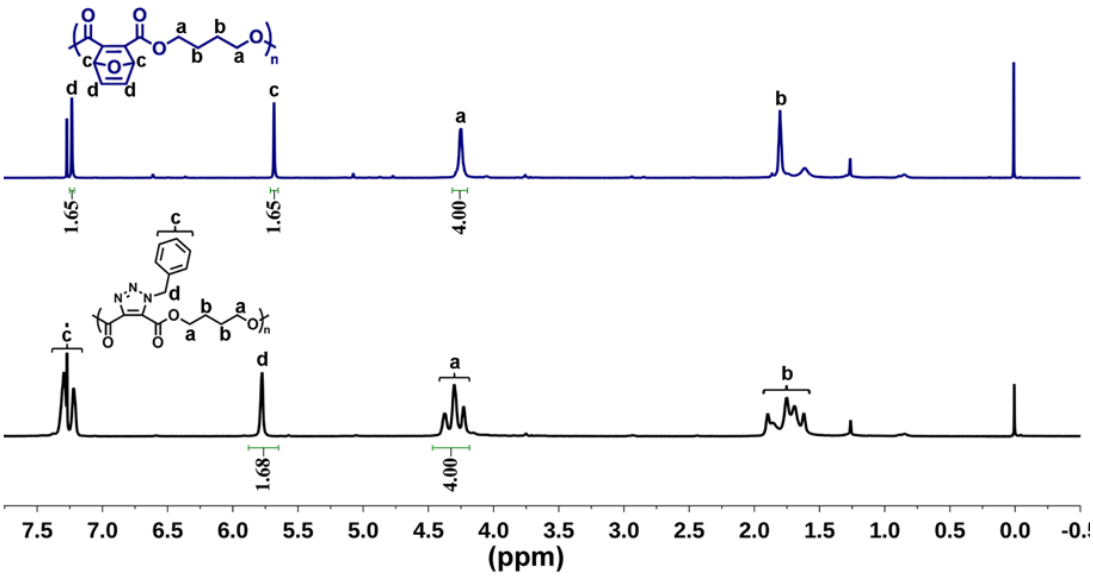


Figure 4.22: ^{1}H NMR spectra of **P8** (up) and **P11** (down) after sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reaction in $CDCl_3$ (500 MHz).

In addition, the efficiency of the sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reactions were found to be 75-79 % from GPC result. GPC analysis exhibited: Mn, $_{GPC}$=6400 g/mol, Mw/Mn=1.73 relative to PS standards in THF at 30°C.

^{13}C NMR also displayed an evidence for successful reaction that two signals at 143,28 and 85.06 ppm assignable to the alkenyl and bridge-head carbons of furan, respectively disappeared and new signals of aromatic carbons appeared in the range of 140-118 ppm (Figure 4.23).

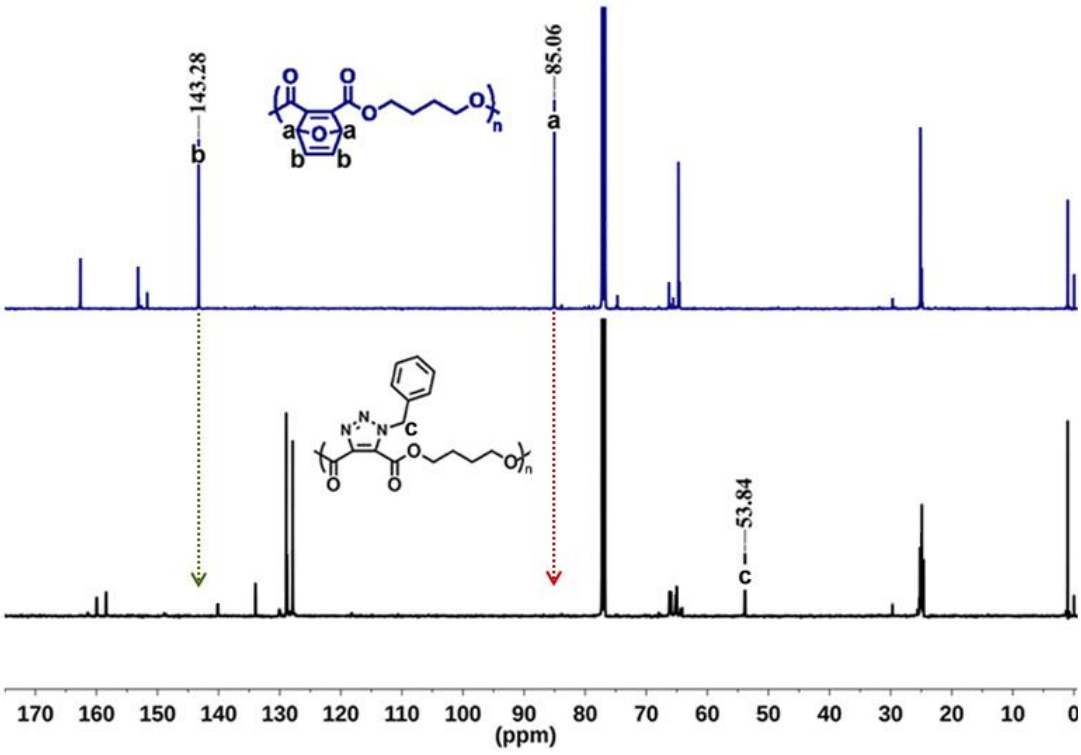


Figure 4.23: ^{13}C NMR spectra of **P5** (up) and **P8** (down) after sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reaction in $CDCl_3$ (125 MHz).

5. CONCLUSION

In this study, firstly we have systematically sythesized different polyesters backbone including reactive alkyne groups in the main chain using various diols. Among this diols, **P1** was selected as model polymer. Secondly, **P1** was reacted with various dienes through Diels-Alder cycloaddition reactions and we have investigated the cycloaddition ability of variety of dienes against the polyester. The **P1** displayed high efficiencies at temperatures ranging from 80 to 120 ^{o}C for 16 h. In addition, 1,3 dipolar cycloaddition was performed with benzyl azide. Oxanorbornadiene functional polymer was previously proven to undergo sequential 1,3-dipolar cycloaddition/retro-Diels-Alder reactions under mild conditions. In line with this idea, **P8** was reacted with benzyl azide at room temperature and it was found that after benzyl azide attack to the double bond between two electron withdrawing carbonyl groups, a rearrangement occurred and furan removed from the structure to produce the final product indicating the sequential reaction was smoothly occurred. It is well-known that the removal of furan from oxanorbornadiene structures requires high reaction temperatures in many other cases [29,65]. But the sequential approach used in this study provides the removal of furan at room temperature.

It should be noted that this type of internal alkyne moiety like in the polyester P1 can become as a potential alternative to alkynes taking place in the SPAAC reactions, because it may be easily introduced into the polymer chain. Additionally, it may be expected that this type of alkyne group can be reacted with nucleophiles, radicals and used in the MCR to yield well- defined more complex macromolecular architectures.

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